

**Epidemiology of human African
trypanosomiasis in western Tanzania**

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Declaration

I, Lucas E. Matemba, do declare that the research described in this thesis is my own work and that it has not been submitted for any other degree or professional qualification except as specified.

Signed..

Dedication

This thesis is dedicated to the memory of my late Mother Eliaingikaya Kowero who set the foundation which is the basis for my success.

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LIST OF ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
AAT	African Animal Trypanosomiasis
BOD	Burden of Diseases
BIIT	Blood Incubation Infectivity Test
CATT	Card Agglutination Test for Trypanosomiasis
CDR	Crude Death Rate
CI	Confidence Interval
CHMT	Council Health Management Team
CSF	Cerebral Spinal Fluid
CTVM	Centre for Tropical Veterinary Medicine
CNS	Central Nervous System
DALYs	Disability Adjusted Life Years
DDT	Dichloro-Diphenyl Trichloroethane
DFID	Department Fund for International Development
DNA	Deoxyribonucleic Antigen
DRC	Democratic Republic of Congo
ELISA	Enzyme-Linked Immunosorbent Assays
EID	Emerging Infectious Diseases
GBDS	Global Burden of Disease Study
GIS	Geographical Information Systems
GLM	General Linear Model
GNI	Gross National Income
GPS	Global Positioning System
HAT	Human African Trypanosomiasis

HCT	Haematocrit Centrifugation Technique
HIV	Human Immunodeficiency Virus
HSR	Human Serum Resistance
HTD	Hospital for Tropical Diseases
HMIS	Health Management Information System
HRUTF	Health Research Users Trust Fund
ITS	Internal Transcribed Spacer
KIVI	Kit for <i>in vitro</i> Isolation of Trypanosomes
LAMP	Loop-mediated Isothermal Amplification
MDG	Millennium Development Goals
MGE	Mobile Genetic Elements
MOHSW	Ministry of Health and Social Welfare
MSF	Médecines Sans Frontières
NGO	Non-Government Organisation
NIMR	National Institute for Medical Research
NTD	Neglected Tropical Diseases
OR	Odds Ratio
PCR	Polymerase Chain Reaction
PTB	Pulmonary Tuberculosis
QBC	Quantitative Buffy Coast
RFLP	Restricted Fragment Length Polymorphism
RR	Risk Ratio
RSS	Rhodesiense Sleeping Sickness

SS	Sleeping Sickness
SIT	Sterile Insect Technique
SRA	Serum Resistance Antigen
SSA	Sub-Saharan Africa
SWG	Scientific Working Group
TB	Tuberculosis
TDR	Research and Training in Tropical Diseases
US\$	United States Dollar
VEO	Village Executive Officers
VSG	Variant Surface Glycoprotein
WBC	White Blood Cells
WCC	White Cell Count
WHO	World Health Organization
YLD	Years of Life Lost
YLL	Years of Life Lived with Disability

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THESIS ABSTRACT

Investigating the Epidemiology of Human African Trypanosomiasis in Western Tanzania

Human African trypanosomiasis (HAT) or sleeping sickness is a debilitating vector-borne disease which is fatal if left untreated. In Tanzania 4 million people, living in rural communities are at risk of HAT; this is a disease of major socio-economical and public health importance. Human African Trypanosomiasis was first reported in Tanzania in 1922. Since then endemicity has been reported in 10 regions of mainland Tanzania, with over 91% of the recent cases reported from only three regions of the western part of the country.

This thesis started by reviewing the existing sleeping sickness historical records in Tanzania aiming at exploring the evidence of *Trypanosoma brucei gambiense* existence in Tanzania.

Historical documentation suggested that probably *gambiense* sleeping sickness did occur in Tanzania. However, there is no enough scientific evidence to confirm the existence of this form of the disease in Tanzania.

This thesis further estimated the under-reporting of *Trypanosoma brucei rhodesiense* in the endemic areas of Tanzania using an established model. Using data from the 2000-2004 outbreak of *T.b.rhodesiense* in Urambo, the model predicted 45% under-reporting. All unreported cases were assumed to be unreported deaths as sleeping sickness is invariable fatal if left untreated. These under-reported findings were then used to recalibrate the burden of *T.b. rhodesiense* (using Disability-Adjusted Life Years – DALYs), as a metric. The burden imposed on rural communities of Tanzania by *rhodesiense* sleeping sickness was found to be high. The costs of hospitalization are also very high considering the long duration of hospital stay (25 days mean hospital stay) for sleeping sickness patients in Urambo.

Finally the thesis investigated spatial and behavioural risk factors for rhodesiense sleeping sickness in Urambo district Tanzania, using a matched case control study both at the village and within the village scales.

Statistically significant clustering was observed at the village level ($P = 0.001$). However there was no significance association in an individual village's analysis. There was an increased risk of sleeping sickness in homesteads with a previous history of sleeping sickness ($P < 0.001$).

CHAPTER ONE:
GENERAL INTRODUCTION

1.1 Neglected Tropical Diseases and Zoonoses

Neglected Tropical Diseases are defined as diseases affecting almost exclusively poor and powerless people (WHO, 2007a). Those affected normally reside in rural areas or urban slums of low-income countries. Often the diseases have been eliminated and forgotten about in wealthier developed countries. NTDs are a group of 14 chronic disabling infections that sometimes kill and often disfigure their victims (WHO, 2008). They include Chagas disease, onchocerciasis, lymphatic filariasis, soil-transmitted helminthiasis, trachoma, Guinea worm, cysticercosis/zoonotichelminths, Buruli ulcer, human African trypanosomiasis (HAT), leishmaniasis, leprosy, yaws and dengue/dengue haemorrhagic fever. Many of these neglected tropical diseases are of parasitic origin with some having a zoonotic reservoir. The World Health Organization (WHO) defines zoonoses as a group of diseases or infections that are naturally transmitted from vertebrate animals to humans (WHO, 1959); meaning that animals play a very important role in maintaining zoonotic infections in nature. There are more than 868 diseases which fall in the category of zoonotic infections; these include those of viral, bacterial, protozoa, helminth and fungal origin (Taylor *et al.*, 2001).

NTDs and zoonoses are devastating obstacles to human settlement and the socioeconomic development of already impoverished communities. It has been documented that approximately 1.2 billion people (~16% of the global population) suffer from one or more NTDs (Balasegaram, 2008; WHO, 2007b) while about 2.7 billion people worldwide subsist on less than \$2 per day (WHO, 2007b). NTDs and zoonoses affect the world's poorest people, they are not subject to compulsory reporting in most of the affected countries, and are therefore not perceived as major public health burdens when compared to other infectious diseases such as HIV/AIDS, tuberculosis and malaria.

Nevertheless NTDs are the most prominent and probably the most devastating public health constraints obstructing the achievement of the Global Health Agenda in the developing world, particularly in most of the sub Saharan African (SSA) countries.

The greatest impact of the neglected diseases is the way they induce poverty, stigmatize, and disable people as well as inhibiting them from being able to care for themselves or their families. Most of these diseases do not lead to epidemiologic emergencies, and consequently attract little attention from the media and the public sector (Balasegaram, 2008). Furthermore, the private sector does not necessarily consider this group of diseases as a lucrative target, a phenomenon which severely hampers spending on research and development of specific drugs, vaccines and diagnostic tools (Trouiller, 2002). As a result they continue to maintain a very low profile in the communities and are often forgotten or left out when most of the public health agendas are formulated (Banerji, 2003; Trouiller, 2002).

There is a grave risk posed by this group of diseases to the world's poorest communities, and the impact these diseases have on those countries in achieving the millennium development goals (MDGs). The MDGs are set of eight goals set by the Millennium Declaration, and adopted by 189 world leaders and signed by 147 heads of state and governments at the United Nations Millennium summit in September 2000; the target of these goals is to eliminate extreme poverty, hunger, and disease by 2015. In realising this global challenge the WHO has grouped NTDs and zoonoses in a category which follows the priorities detailed below in order to enable proper planning of strategies to enhance control and eventually eliminate some of these diseases (WHO, 2007a). Success in developing strategies which would enable the control of these groups of diseases will have a direct impact in achieving several Millennium Development Goals. These were further sub divided into "tool-ready" and "tool-deficiency" categories.

The tool ready category includes those diseases for which powerful and inexpensive control tools are currently available. The second category is the diseases which rely on costly and difficult-to-manage tools. A good example of tool deficiency diseases is HAT.

1.2 Global Burden of Neglected Tropical Diseases

Reliable epidemiological data are lacking in most of developing world, particularly SSA. In realization of this short-fall the World Bank and World development report on investing in health recommended the use of cost effective intervention packages for countries under different levels of development (World Bank, 1993). The Global Burden of Disease (GBD) study was therefore developed with the help of Harvard University under the sponsorship of WHO in collaboration with a global network of over 100 scientists (Murray and Lopez, 1996a; World Bank, 1993). The principal aim was an attempt to assess in an objective manner using a global scale, the importance of different conditions that result in adverse health outcomes, with the aim of prioritizing interventions. The study used a standard unit of health metric measure, disability adjusted life years (DALYs). The results which can easily be incorporated in comparing cost and effects of different interventions aimed at reducing the burden of disease. DALYs is the sum of years of life lost due to premature mortality (YLL) and years of life lived with disability (YLD) (Lopez *et al.*, 2006). The public health burden imposed by HAT was estimated to be 1.5 million DALYs in 2002 (WHO, 2004); the disease is ranked second and fourth amongst the most important vector-borne diseases in Africa in terms of mortality and DALYs respectively (Lash and Aschengrau, 1999). The global figure for the burden for sleeping sickness, calculated using a conservative estimate of 50,000 cases per year, is 1.78 million DALYs per year (Murray, 1994)

1.3 Trypanosomiasis; The Disease and Aetiology

HAT which is also known as sleeping sickness, is a severe debilitating disease which is always fatal if left untreated. The disease in humans is caused by *Trypanosoma brucei rhodesiense* and *Trypanosoma brucei gambiense*.

It is the most complex of the endemic tropical diseases, it flourishes in impoverished rural parts of Africa, where it is estimated to affect some 70,000 people in SSA (Garcia *et al.*, 2006). The disease is spread through the bite of infected tsetse flies (*Glossina* spp.). HAT is the third most important vector borne disease behind leishmania (Molyneux *et al.*, 1996). Around 300,000 – 500,000 people are thought to be infected with HAT, with the mortality rate estimated to be approximately 50,000 annually (WHO, 2004). A few days following a bite of an infected tsetse a painless nodular skin lesion or chancre develops, lasting for about fourteen days. During this initial stage (early stage), there is marked generalized body malaise, fever and sometimes a satellite lymphadenopathy. Later as the trypanosomes invade tissue fluids, lymph, blood and bone marrow one may experience a transient local oedema, sensational hyperaesthesia (Kerandels sign), intermittent fever sometimes accompanied by headache, pains in the joints, splenomegaly and lymphadenopathy (Apted, 1970). As the disease progresses further to the meningo-encephalitic stage (late stage), the parasites invade the cerebrospinal fluid (CSF) and brain tissues. The disease progressively leads to a variety of clinical manifestations, including headache, irritability, tremors, ataxia, convulsions, change in personality, somnolence particularly during the day time, pronounced wasting and finally may end up in coma followed by death in the absence of treatment (Dumas, 1988).

1.3.1 Trypanosomes; The Causative Organism

Trypanosomes are group of kinetoplastid protozoan parasites, belonging to the subphylum *mastigophora*.

The trypanosomes of medical importance are *Trypanosoma cruzi*, which causes Chagas disease in South America, and *Trypanosoma brucei* s.l., which causes trypanosomiasis in SSA.

1.3.2 Classification

Trypanosomes are classified under the sub-kingdom protozoa, phylum Sarcomastigophora, order Kinetoplastida, family Trypanosomatidae and genus *Trypanosoma*. This genus has two groups, Salivaria and Stercoraria. Transmission is either by inoculation of metacyclics with the saliva (Salivaria) or by contamination of mucosa or broken skin with trypanosomes in the vector's faecal material (Stercoraria). Within the Salivaria the main subgenera are: *Duttonella* (species: *Trypanosoma vivax*, and *Trypanosoma uniforme*); *Nannomnas* (species: *Trypanosoma congolense* and *Trypanosoma simiae*); and *Trypanozoon* (species: *T. brucei*, *T. evansi* and *T. equiperdum*) (Hoare, 1970). *T. vivax* and *T. congolense* are the main causes of disease in domestic cattle in SSA.

Mechanical transmission may occur in situations where a biting insect passes the infection from an infected to an uninfected animal in the course of interrupted feeding. This model of transmission has proved to be sufficiently effective in maintaining *T. vivax* and *T. evansi* in South and Central America, and the latter species in North America and Asia (Sumba *et al.*, 1998). However, the time elapsed between feeds plays a crucial role for effective transmission, because trypanosomes die as soon as blood dries. Also large biting insects such as tabanids and even tsetse flies are more likely to act as mechanical vectors as they carry relatively large volumes of blood. Mechanical transmission may also occur when dogs, cats and wild carnivores feed on fresh carcasses infected with trypanosomes (Laveran, 1906; Moloo *et al.*, 1973).

The salivarian group are the only pathogenic trypanosomes that cause sleeping sickness in man and nagana in domestic animals in endemic countries of SSA. In man the disease is caused by *T.b. rhodesiense* and *T. b. gambiense*. The remaining species cause disease in animals, but are not infective to humans due to their sensitivity to human serum that hinders their survival in man.

However, the disease is possible for individuals lacking lytic factor, this has been reported recently in India (Joshi, 2005)

1.3.3 The Life Cycle of Trypanosome

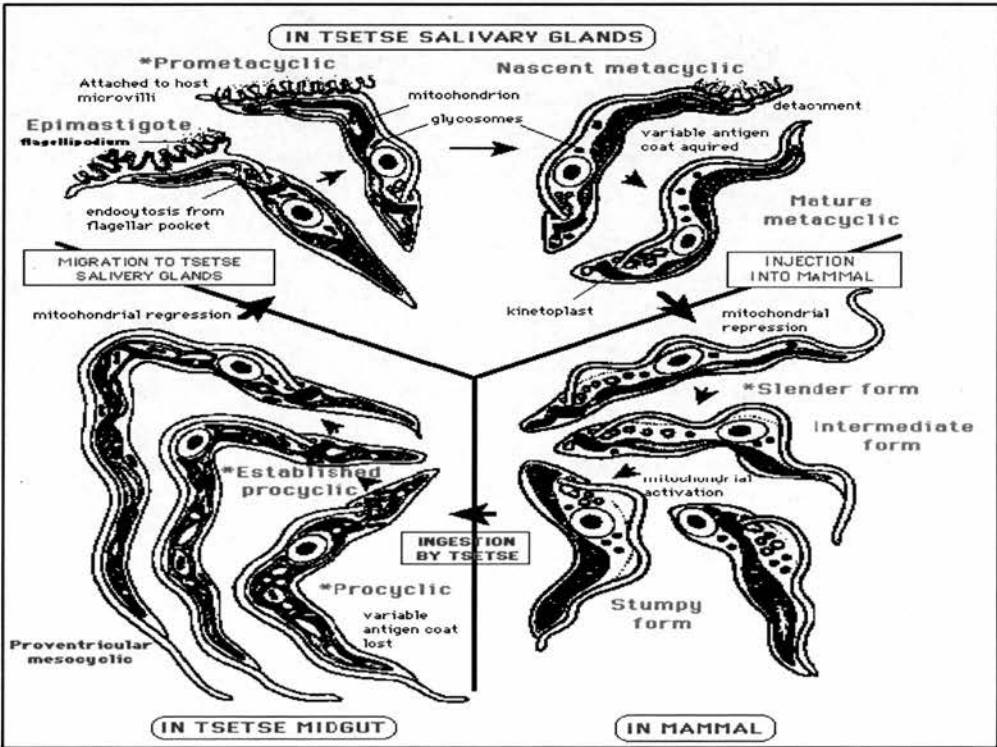
Tsetse flies are the only known vector for *Trypanosoma brucei*. There are about 31 species and subspecies of tsetse flies present in Africa, but only some of them are capable of transmitting trypanosomes. Their life span varies from an average of one to six months. They prefer mostly warm, humid and shady areas. Parasites are ingested from an infected mammalian host by the tsetse fly which if susceptible remains infective for life. However, only a small number of infected tsetse flies can maintain high levels of relative transmission cycles. Tsetse flies take up trypanosomes from the host during feeding. The trypanosomes pass through the midgut then penetrate the gut wall and migrate to the ectoperitrophic space.

Once in the ectoperitrophic space between midgut epithelium and the peritrophic membrane, the stumpy form trypomastigotes transform to procyclics. Only small proportions of tsetse flies which have taken up trypanosomes develop a mature infection and it takes about 3-4 weeks. Available documentation shows that only teneral flies are capable of developing a mature infection. Although there is no clear explanation for this, currently available research findings suggest that, low levels of gut lectin present in newly eclosed flies, and also poorly developed peritrophic membrane play role in making the teneral flies more susceptible to trypanosome infection (Lehane and Msangi, 1991).

In an established infection procyclics move to the proventriculus after rapid proliferation which takes about 10-12 days, and subsequently migrate as epimastigotes via the hypopharynx to the salivary glands. Development is complete once the trypanosomes develop through the epimastigote stage becoming mammalian-infective metacyclic trypanosomes which can take up to 28 days. Figure 1.1 shows various *T. brucei* morphological stages.

Transmission occurs when mammalian host is bitten by infected tsetse during feeding. During tsetse feeding metacyclic trypanosomes are injected into the dermal tissue of the mammalian host. The metacyclics rapidly transform into long slender bloodstream forms (BSF), which then multiply by binary fission and subsequently invade the lymphatic, blood system and later the central nervous system. Beside the long slender forms, morphologically different, non-proliferating stumpy forms are observed at peak and declining parasitaemia in the blood of the host. It is these stumpy forms are able to continue the life-cycle in the insect vector.

Figure 1.1 The diagram showing human infective trypanosome developmental cycle in mammal and in the tsetse fly vector (Vickerman, 1985)



A number of hosts have been identified to be harbouring trypanosomes varying from domestic and wild vertebrates.

Among the vertebrate hosts are mammals both domestic such as cattle ((Maudlin *et al.*, 1990; Onyango *et al.*, 1966; Stephen, 1970a) and wild mammals such as bushback (Heisch, 1958), amphibians and fish (Connor 1989), reptiles such as Monitor lizards (Njagu *et al.*, 1999) and avians (Apanius, 1991).

1.3.3.1 Wild Hosts

It is known that wild hosts play an important role in maintaining trypanosomiasis (Heisch, 1958; Kinghorn, 1925). The fact that a large number of wild animal hosts are known to harbour infection, but do not develop the symptoms of disease suggests they may play a role as reservoir hosts. The most important host among the wild reservoirs are animals such as bushback (Heisch, 1958), bovids and suids (Geigy, 1971), hartebeest (Geigy, 1971), hyena (Awan, 1971, 1979; Geigy, 1971), warthogs (Awan, 1971, 1979), zebra (Mulla, 1988), waterbuck (Awan, 1971, 1979; Geigy, 1971) and lions (Geigy, 1971). Historically, bushback is among the most remembered in the epidemiology of trypanosomiasis among the wild animal host due to the fact that the first human infective trypanosome was isolated from this species (Heisch, 1958).

1.3.3.2 Domestic Hosts

Bruce (1910) showed by injection of an infected blood sample from a domestic cow into a monkey that cows could act as reservoirs of infection. Since then a number of domestic hosts such as cattle (Gibson, 1983; Onyango *et al.*, 1966; Robson, 1973; Stephen, 1970b; Welburn *et al.*, 2001b), goats (Stephen, 1970b), sheep (Fairbairn, 1948; Stephen, 1970b), dogs (Gibson, 1983) and pigs (Okuna *et al.*, 1986; Stephen, 1970b) have been identified as important hosts for trypanosomes.

It is worth pointing out that despite the fact that domestic animals have been identified as important hosts for trypanosomes; they respond differently to infection depending on a number of factors such as breed of animal; in West Africa for example the Zebu cattle are more susceptible than the dwarf breeds such as the N'dama and Muturu, in East Africa on the other hand, pure-breed and grade animals are more susceptible to trypanosomiasis than the indigenous cattle (Stephen, 1970b).

Several other factors are believed to play part in influencing the clinical manifestation of trypanosomiasis these include; nutritional condition of the animal, concomitant viral, parasitic or bacterial infection, stressful condition resulting from vaccination, trekking, thirst and finally climatic condition such as unstable temperature (Stephen, 1970b).

In Tanzania, there have been a number of studies conducted to show the association between domestic animal reservoirs and sleeping sickness. During the Tinde experiments a number of *T. b. rhodesiense* strains were continuously passaged through domestic animals, and even after several years still maintained their infectivity to humans. (Ashcroft, 1959; Corson, 1936; Fairbairn, 1948)

1.4 Epidemiology of African Trypanosomiasis

HAT has probably existed in East Africa for many centuries but the disease itself was not described until the late 19th early 20th century by European colonialists (Hide, 1999). Among the two protozoan subspecies, *T. b. gambiense* and *T. b. rhodesiense*, the latter is the least investigated of sub species and is the main focus for this thesis; this parasite is found in eastern and southern Africa causing acute illness lasting for several weeks.

The epidemiology is complex and transmission cycles are subject to interaction between humans, tsetse flies and the animal reservoirs both domestic and wildlife.

In Eastern Africa, *T. b. rhodesiense* is the species responsible for human disease, and the main reservoirs are both domestic and wild animals (Fevre *et al.*, 2001; Onyango *et al.*, 1966). Since animal reservoirs play an important role in transmission, understanding the epidemiology of *T. b. rhodesiense* in humans as well as in its animal reservoir is essential for the accurate prediction of effective control options for HAT (Coleman and Welburn, 2004).

The fact that trypanosomiasis affects both humans and animals, trypanosome parasites are a dual constraint to human and animal health, and as such, have serious impact on rural livelihood. Studies conducted in both East and West Africa have shown that there is a substantial percentage of domestic animals which are reservoirs of human infective trypanosomes (Mehlitz *et al.*, 1982; Robson, 1973). Further studies confirmed that domestic cattle and their demographic characteristics are major risk factors for the spread of human infective parasites. In this context targeting treatment of domestic cattle is seen as an important method for controlling human disease (Fevre *et al.*, 2001). Such treatments also have significant impact on the cattle trypanosomes, resulting in improvements in animal health. Hence effective control measures for HAT can only be achieved through controlling the causative vectors (see later) as well as providing necessary treatment to all affected humans as well as identifying and providing treatment to all potential reservoir hosts in the respective area.

In *T. b. gambiense* disease, the classical human-fly-human transmission cycle occurs in both endemic and epidemic situations (Committee., 1998; WHO, 1998).

Difficulties in differentiation of *T. b. brucei* and *T. b. rhodesiense* have led to controversies over the importance of reservoir of the infection of human disease in both domestic livestock and wild animals. The development of blood incubation infectivity test (BIIT) by Rickman and Robson (1970), which test the parasites ability to survive challenge with human serum in mice models, plays a very big role in distinguishing the two sub-species. The test was developed based on the theory that *T. b. brucei* can not survive after five hours incubation in human serum at 37°C (Rickmann, 1970). This test was later modified further by Awan and Dillmann (1973).

The potential human infective trypanosomes have been successful isolated using BIIT technique in studies conducted in Uganda (Enyaru, 1992; Kakaire *et al.*, 1993; Okuna *et al.*, 1986).

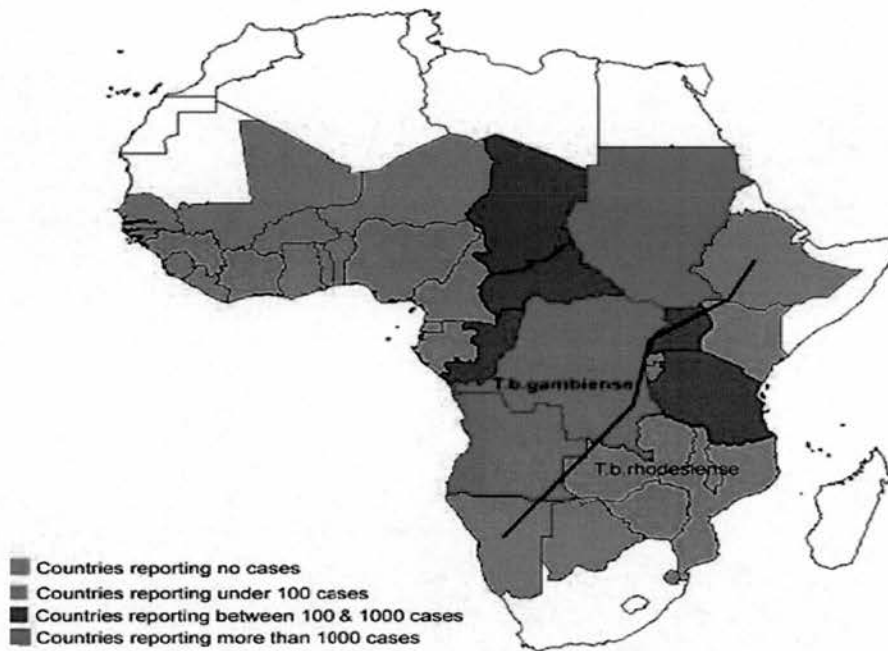
In more recent studies using BIIT, Waiswa *et al* (2003) demonstrated that a wide range of domestic livestock (including pigs), harbour human infective trypanosomes (Waiswa *et al.*, 2003).

1.4.1 Distribution of Trypanosomes in Sub Saharan Africa

The distribution of trypanosome-infected and potentially infected livestock in SSA is closely related to that of the tsetse species of the genus *Glossina*.

The distribution is also limited by ecological conditions varying from 14° North from Senegal (West Africa) to 10° North in Somalia (Eastern part of Africa) and Latitude 20° S, to the northern fingers of Kalahari and Namibia deserts. This covers about 11 million km², over 37 countries, including half of the available arid land. Meaning that climatic conditions, temperature and ecological vegetation are very important parameters in determining the distribution of the tsetse (Molyneux *et al.*, 1996). Figure 1.2 shows disease distribution of HAT across Africa.

Figure 1.2 Map showing the distribution of human African trypanosomiasis



Savannah species (those of the Morsitans group) are good vectors of pathogenic trypanosomes of livestock. Population of savannah species feed mainly on mammalian hosts, particularly bovids such as the buffalo's as well as antelope, cattle, sheep, goats and suids such as bush pigs and warthogs. In contrast the riverine tsetse (those of the Palpalis group) prefers a wide range of hosts including reptiles and humans. The major difference between suids and bovids is that the former infect flies particularly with *T. simiae* and *T. godfreyi*, while bovids are mainly source of *T. vivax* and *T. congolense*. The epidemiology of non tsetse-transmitted trypanosomiasis such as *T. evansi* is influenced by several factors such as seasonal outbreaks, whereby biting flies in this case (Tabanids, Stomoxys and others) are influenced by important seasonal climatic differences. The epidemiology is also influenced by host preferences and diurnal behaviour patterns of the various local species of tabanids and other biting flies.

The distribution of two forms of the diseases (Gambian and Rhodesian) can also be easily separated by their geographical location.

The Great African Rift Valley forms a rough boundary between the eastern distribution of the *T. b. gambiense* and the western distribution of the *T. b. rhodesiense* (Welburn *et al.*, 2001a). More techniques have been developed to discriminate the strains of trypanosomes using isoenzyme characterization (Gibson, 1983), and polymerase chain reaction (PCR) the move which made it possible to study the origin of the disease, the epidemic development and maintenance (Fevre, 2001; Fevre *et al.*, 2001; Picozzi *et al.*, 2002).

1.5 Diagnosis of Human African Trypanosomiasis

Although there are some differences in the techniques that are used to diagnose HAT most of the presenting symptoms are very similar. However, it is very important to be able to tell the two infections apart, as the clinical course of Rhodesian sleeping sickness is much faster than in Gambian sleeping sickness.

In Rhodesian sleeping sickness death can occur within four to six months of infection whereas it can take years for this to happen with the Gambian form. Presently the most commonly used tests in the field are microscopy using thin or thick blood films, micro haematocrit centrifugation techniques (HCT) or Woo test (Woo, 1970), Mini Column or Quantitative Buffy Coat (Murray *et al.*, 1977) and CATT test, which are believed to increase the sensitivity of trypanosome detection by several orders of magnitude (WHO, 1986).

1.5.1 Clinical Diagnosis

Generally, the clinical diagnosis of sleeping sickness is very difficult due to the fact that there is no single feature which can be regarded as pathognomonic for the disease; moreover HAT presents in a similar way clinically to a number of other infectious diseases. This situation makes it difficult for clinicians to make immediate diagnosis based on signs and symptoms presented by the patient.

Therefore proper diagnosis relies on a number of tests including parasitological and serological. In the case of positive serology results, parasitological confirmation is also required.

1.5.2 Parasitological Diagnosis

Parasitological diagnosis relies upon demonstration of parasites in the blood, lymph and glandular aspirates or cerebral spinal fluid (CSF). Sometimes, due to periodicity of parasitaemia, the number of parasites may sometimes be very low, in these cases multiple sampling and concentration techniques are often necessary in order to detect the parasites. This is particularly common with *T. b. gambiense* due to scarcity and infrequent appearance of the parasites in the blood.

In line with all above listed diagnostic methods, stage determination is one of the most important aspects in the diagnosis of HAT as it determines the line of treatment. This is determined using WHO criteria, where lumbar puncture is performed and cerebral spinal fluid (CSF) obtained and is mainly based on the white cell count (WCC) or protein content. Consequently the diagnosis of late stage trypanosomiasis is reached upon one of the following criteria (WHO, 1998): CSF WCC > 5 cells/ μl or the total CSF protein > 37 mg $(100\text{mL})^{-1}$ (as measured by dye-binding protein assay) or both criteria with or without the presence of trypanosomes in the CSF. It has been, however, documented that the presence of white blood cells in the CSF is by itself sensitive enough for the diagnosis of central nervous involvement as the combination of above criteria Miézan *et al.* (1998). In first stage HAT, all the CSF parameters are absolutely normal. That means CSF WCC absent or less than 5 cells/ μl , and the absence of proteins in the CSF (WHO, 1998). In rural areas where most of the cases occurs, under field conditions and in less specialized laboratories and in most of the rural areas, stage determination is usually conducted using direct examination of CSF for the presence of trypanosomes.

Also in order to increase the sensitivity, the CSF sample can be centrifuged (Cattand and de Raadt, 1991; Woo, 1970). CSF protein can be quantified using either precipitation or the calorimeter method.

1.5.3 Serological Diagnosis

A number of serological tests have been developed for the diagnosis of HAT, including: latex agglutination test (Buscher *et al.*, 1999), enzyme-linked immunosorbent assay (ELISA) test (Buscher *et al.*, 1999; Luckins, 1977; Nantulya, 1988; Nantulya *et al.*, 1992) and card agglutination test for trypanosomiasis (CATT) (Magnus *et al.*, 1978).

CATT which is the most commonly used today is a rapid, simple agglutination assay for *T. b. gambiense* specific antibody, which uses antigenic reagent based on *T. b. gambiense* variable antigen type LiTat 1.3.

A field CATT kit is available and the test is rapid and easy to perform, allowing several hundred people to be screened in a day, the test is highly sensitive (Moore and Richer, 2001), however, a number of false positives have been reported in Uganda and southern Sudan ((Moore and Richer, 2001; MSF-DND, 2001). CATT is most commonly used as a primary diagnostic test for Gambian sleeping sickness. However, a confirmatory test using parasitological means is always necessary. Nevertheless CATT still reduces the workload of conducting parasitological tests in all individuals under survey limiting conditions. In that, only CATT positive individuals need to be tested by microscopy. However, in areas afflicted with *T. b. rhodesiense*, no serological tests are currently available, All these serological methods have been found to be more sensitive than most of the parasitological diagnostic techniques used today, nevertheless most of the serological tests are not able to distinguish between active infection and a past treated infection (Van Meirvenne *et al.*, 1995). However, the positive thing about these tests is that they can be used to detect relapse infections in trypanocidal drug therapeutic studies for the periods when it is not possible to isolate parasites from peripheral blood (Rae, 1989). Other serological

diagnostic techniques are the immune trypanolysis test (Van Meirvenne *et al.*, 1995). Both ELISA and immune trypanolysis methods are important and are very useful in situations where good laboratory facilities exist particularly in large epidemiological surveys but are not practical for field application (Buscher and Lejon, 2004).

1.5.3 Molecular Diagnosis

Molecular techniques which include PCR (Kanmogne *et al.*, 1996; Kyambadde *et al.*, 2000; Penchenier, 2000), and the newly developed loop mediated isothermal amplification (Buscher and Lejon, 2004; Notomi *et al.*, 2000) are advanced technologies which are based on studying the DNA signals in a sample.

However, due to the costs and specialized equipment required for PCR, and LAMP still being under evaluation they are not presently available in most of the laboratories in disease endemic countries.

A number of advanced molecular based techniques have been developed which detect unique trypanosome species and strains. Techniques such as isoenzyme characterization (Gibson, 1983; Tait, 1980), restricted fragment length polymorphism (RFLP) (Hide, 1991, 1994), the PCR amplification technique using minisatellite markers analysis (MacLeod *et al.*, 2000) and the analysis of variability in mobile genetic elements PCR (MGE-PCR) (Tilley, 2003). While a PCR reaction specific to the gene that results in human serum resistance in *T. b. rhodesiense* allows identification of this parasite from samples of both *T. b. brucei* and *T. b. gambiense* (Welburn *et al.*, 2001b). This amplification has recently been improved on by Picozzi *et al.* (2008) who designed a multiplex incorporating a single copy gene present in *T. brucei* s.l. The inclusion of GPI-PLC as an internal control indicates whether sufficient genomic material is present in the PCR reaction for the detection of a single copy gene. Recently primers have been designed to the internal transcribed spacer gene and the use

of a nested PCR (Cox *et al.*, 2005) allows the identification of all clinically important trypanosomes in single PCR.

1.5.4 Loop-Mediated Isothermal Amplification (LAMP)

Loop-mediated isothermal amplification or LAMP is a novel DNA amplification technique, developed recently in by a Japanese company called Eiken Chemicals (Notomi *et al.*, 2000). LAMP promises hope for the solution of the difficulties encountered for the sensitive diagnostic tool for HAT in rural areas; it does not require high precision thermal cycler equipment, gel electrophoresis or a UV illuminator.

Meaning that, neither amplification nor detection requires expensive or sophisticated equipment that would restrict its utilization to modern and well equipped laboratories.

Most importantly, the technique is highly specific, rapid and efficient and has several advantages as compared to traditional molecular tools. It is documented that amplification occurs in less than one hour and may even take less than 30 minutes (Nagamine 2002). The LAMP reaction proceeds under isothermal conditions, (between 60 to 65°C), which can simply be maintained using water bath, and it does not require purified DNA for efficient DNA amplification. DNA can be amplified directly from heat treated blood samples as well as CSF and normal serum (Poon *et al.*, 2005; Njiru *et al.*, 2007). This makes the technique one of the most cost effective molecular tools as it removes the need for DNA extraction step, which is time consuming and also very costly.

1.6 Control of Human African Trypanosomiasis

Despite significant advances in technology, the control of HAT which used to be a top priority during colonial era remains a nightmare. This is probably due to a number of factors with the major one being political instability in most of

the affected countries which followed after independence gained in early 1960s (Pepin and Meda, 2001). It is clear that *T. b. gambiense* and *T. b. rhodesiense* are harboured within different mammalian reservoir hosts, and as the clinical progression of the two parasites also presents differently, it is obvious that even the control strategies will be different. The control of gambiense HAT which is probably less complicated relies entirely on case detection and treatment provision mainly using active case finding. On the other hand the active case finding in the control of rhodesiense HAT is less important due to unavailability of sensitive diagnostic facilities, moreover an additional effort is necessary to control the infecting parasites in the animal reservoirs. However, principally most of the control strategies are more or less the same for both parasites and are detailed below.

1.7 Treatment of Human African Trypanosomiasis

The control of HAT depends mainly on chemotherapy, with effective treatment entirely determined by proper stage determination of the disease.

The currently available treatments for HAT, particularly the Rhodesian form depends entirely on a narrow choice of drugs that came on the market over 50 years ago. The situation is not much better in the treatment of the Gambian form; however, a new drug has come on the market in the last 20 years. The drugs tend to be scarce, in some cases highly toxic, difficult to use and patients require hospitalization. Moreover there are increasing reports of resistance (Croft, 1999; Matovu *et al.*, 2001) to all drugs used to treat HAT. The treatment for early stage infections of the disease entirely relies only on two drugs, pentamidine and suramin for gambiense and rhodesiense respectively, although suramin can be used for the treatment of early stage gambiense, pentamidine is preferred for the treatment of *T. b. gambiense* today. Melarsoprol remains the drug of choice for the treatment of late stage of both forms of sleeping sickness. Melarsoprol developed in 1949 is a fast acting drug, capable of eliminating the parasites from the blood and lymph within 24 hours of treatment in most cases,

however, this drug is highly toxic most commonly recorded side effect been encephalopathic syndrome which occurs in 5-7% of all treated cases with fatality of 10-70% of those patients (Commitee., 1998; Pepin and Milord, 1994; WHO, 1998). For those with the Gambian form of the disease where melarsoprol treatment has failed, eflornithine can be used. However, eflornithine has many drawbacks which limit its use on a large scale (Kuzoe, 1993). Its mode of administration is complicated requiring a large dose of 400 mg/kg/day administered intravenously in four equal doses which are administered every 6 h for 14 days in a hospital. The cost of treatment per patient has been estimated at US\$500 (US\$210 for drugs, US\$200 intravenous fluid, perfusion kit, and US\$70 costs of hospitalization).

However, despite the eflornithine providing the best alternative therapy to melarsoprol for gambiense sleeping sickness, it is ineffective alone against *T. b. rhodesiense* infection (Kuzoe, 1993).

Treatment failure due to sleeping sickness has been reported in several countries, most of them being gambiense endemic countries including Uganda (Hutin *et al.*, 2004) and southern Sudan (Hutin *et al.*, 2004; Moore and Richer, 2001). However, treatment failure may be a result of several factors, the most important ones been patient's immune system, parasitic drug resistance and individual variation to infection. It is worth mentioning that patient immune system is a very important factor the treatment of HAT in most of the disease endemic countries, it is known that, proper functioning immune system is important for fast healing from any disease condition. Most of the HAT endemic countries face a major infectious disease challenge such as human immunodeficiency virus (HIV), which suppresses body immunity, and therefore contributes to treatment failures. There are very limited studies to show relationship between HAT treatment and HIV particularly rhodesiense HAT, but available studies show that HAT patients co-infected with HIV respond very poorly to eflornithine treatment (Pepin *et al.*, 1992).

In animal African trypanosomiasis, the use of drugs for the prevention and treatment of the disease has been important for decades (Leach and Roberts). The only concern is the development of resistance to these commonly used drugs by the parasite. The most widely used chemoprophylactic drug and also the least expensive is isometamidium chloride, (Eisler *et al.*, 2003). This drug has been in use for over 20 years and it gives a protection of 3-6 months against all the three animal African trypanosome species. Other drugs which have proven to be effective for the control are Ethidium, Presidiums, Homithidium bromide and Diminazene aceturate (Berenil®, Hoechst Germany). Diminazene aceturate is also effective against all the three forms of animal African trypanosomes.

However, the development of resistance to these drugs has been widely reported in East Africa (Eisler *et al.*, 2003; Kibona *et al.*, 2006; Mulageta *et al.*, 1997; Shinyangwe *et al.*, 2004). Nevertheless, apart from the widespread resistance observed to these drugs, and also despite their extensive use in disease control, the drugs are expensive and time consuming to administer, hence they are not seen as suitable options for long-term use in solving the problem of animal African trypanosomiasis.

1.7.1 Immunological Control

Attempts to develop a reliable vaccine against African trypanosomiasis have been an unachievable dream as parasites ability to change the composition of its exposed surface antigen. Since the conventional approaches to the control of the disease have largely met with failure, there has been renewed interest in identifying novel aspects of the biology, chemistry and molecular biology of trypanosomes that might be exploited to develop new targets for the vaccine. If developed, then vaccination could form the best option for this disease (Hadjuk *et al.*, 1992).

1.7.2 The Trypanosome Variable Surface Glycoprotein (Vsg)

The surface of both the metacyclic trypanosomes that enter the mammal during tsetse fly meal and the subsequent proliferating bloodstream forms are covered with a mono-layer of a variable surface glycoprotein (VSG). The VSG forms a barrier between conserved protein in the cell membrane and the effectors molecules of the host immune system (Sayed 2000).

Once host antibodies that recognize any one VSG reach a high enough titre the trypanosomes expressing that particular VSG are killed.

The persistence of an infection, despite the host mounting an immune response, is dependent on antigenic variation of the VSG (Cross, 1978). This occurs through stochastic changes in which a single VSG gene is expressed from repertoire of possibly a thousand. The long term persistence of *T. brucei* infection, for example, is dependant on evasion of the host immune response through a complex system of antigenic variation based on the VSG which forms a protective mono-layer over the cell surface. The switch in VSG expression occurs either through gene conversion of the active VSG expression site or through inactivation of one VSG expression site and activation of one of the ~20 other VSG expression sites.

1.7.3 The Use of Trypanotolerant Animals

Some breeds of indigenous domestic animals, especially cattle have significant degree of trypanotolerance and are capable of thriving in tsetse infested areas, where susceptible breeds cannot survive (Shaw and Hoste, 1987). Increasing the number of such trypanotolerant animals may result in a significant reduction in the number of new infections and hence resulting in control of trypanosomiasis in livestock. Such cattle have been imported into countries such as Gabon and Democratic Republic of Congo (DRC), where they are successfully being raised on several large ranches (Shaw and Hoste, 1987).

However, despite trypanotolerant animals offering a considerable potential as an alternative means of raising cattle in tsetse infested areas, they currently represent only 5% of the cattle population in SSA. Therefore their limited availability and because of their small size, they are not preferred by farmers who always aspire for better products. This is probably why wide scale programmes have been limited.

1.7.4 Vector Control

To date, a variety of methods have been used in an attempt to reduce the tsetse fly populations. These include the use of insecticides applied on odour-baited traps or applied as aerosols by aerial or ground spraying (MacLennan, 1980). Cattle dipping or pour on is another method used to kill tsetse. In this method insecticides such as deltamethrin which is capable of killing up to 100% of alighting flies within two weeks are used. However, in order to achieve sufficient outcome with this technique, domestic livestock must be present in the area in sufficient numbers, with cattle representing a highest proportion of the host complex and most of the cattle have to be presented for treatment on regular basis. Unfortunately, the cost of insecticides is a serious constraint for the sustainability of this method (Eisler *et al.*, 2003). In recent years the use of insecticides such as DDT and dieldrin has lost favour among tsetse control institutions due to environmental concern.

Also treated areas are easily re-invaded necessitating costly re-treatment programmes. Furthermore, all these methods do not provide immediate cattle protection from being infected by trypanosomes.

1.7.5 Sterile Insect Technique

Theoretically, the low reproductive capacity and infrequent mating of the female tsetse flies makes them ideal candidates for control by genetic techniques. The sterile insect technique (Shaw and Hoste, 1987; Shaw) involves the release of male flies that have been sterilized by gamma irradiation into the environment to compete with the wild males in mating (Cossman *et al.*, 2003). This method has proved successful in Zanzibar where *Glossina austeni* males sterilized by gamma irradiation were dispersed by air over the whole island in 1994. No wild tsetse has been caught since September 1996. Eradication of *G. austeni* from Zanzibar was declared at the end of September 1997 (Saleh *et al.*, 1998).

However, this method has many pitfalls, including the enormous costs of implementation, low density of target population required for the SIT to be effective (Politzar and Cuisane, 1998) and also the method works best in isolated areas in order to avoid re-invasion by new migrant flies.

1.7.6 Environmental Control

Environmental control can also be used to reduce tsetse populations. These were popular in the early stages of the 20th century and include Bush clearing and elimination of wild animals which may act as reservoirs of disease. However, these measures have been declared environmentally unsound as although bush clearing makes the habitat unsuitable for tsetse habitation; this method has disadvantages, including decrease in soil fertility, soil erosion and adverse effects on water supplies. Whereas elimination of wild animal hosts is not popular method as African economies rely on tourism industry as a source of foreign income and wild animals are among the major attractions for tourists.

1.7.7 Biological Control

Biological control involves the use of natural enemies of the tsetse vector such as parasites and predators like fungi, bacteria and parasitic mites. In order to be successful, biological control organisms generally have to originate from a different geographical or ecological area from the potential pest to be controlled. Otherwise it would be expected that the control and target organisms would be sufficiently adapted to one another that no significant degree of control would be easily maintained over a long period of time. Most trials of parasites on tsetse flies have used insects that occur naturally in tsetse habitats, which may partly explain the lack of success.

Bacteria and fungi have been used in experimental studies to show that they could be potential candidates for the control of trypanosomiasis. These include *Pseudomonas aeruginosa*, *Serratia marcescens* and *Bacillus sphaericus*, (Kaaya and Darji, 1989). The advantage of using biological control methods includes the fact that they do not affect the environment negatively and it is a self-sustaining method. Once the entomopathogens are introduced in the environment, they will multiply and attack their intended targets naturally. There are, however, a few shortfalls such as the difficulty in choosing a suitable method of formulating and dispersal of the pathogens and the chances of adaptation of the insect target to the pathogen-host relationship, (Kaaya and Darji, 1989).

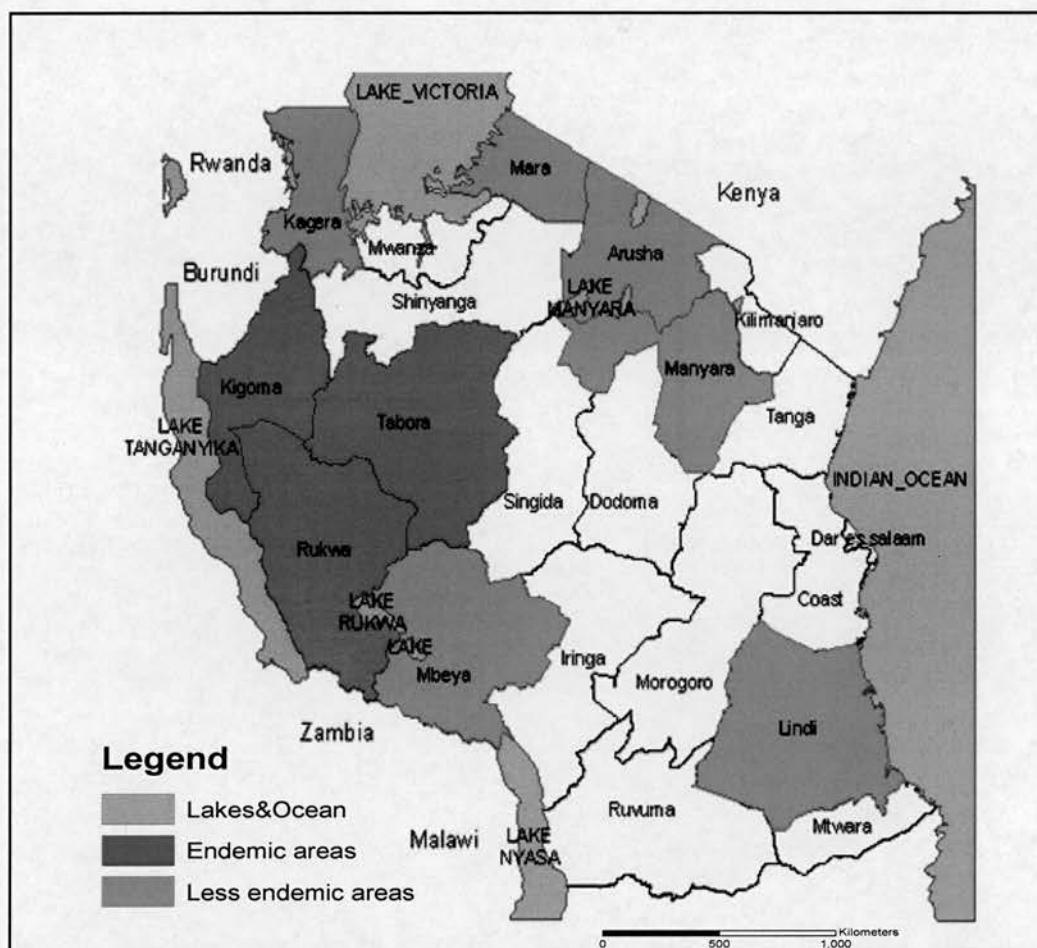
1.8 Sleeping Sickness in Tanzania

In Tanzania, HAT remains a major socio-economic and serious public health problem in rural communities. Four million people are at risk which can cause a big development crisis that affects many sectors. It has drastically affected human and animal health, economic and social progress reducing life expectancy of rural communities and deepening poverty.

Available documentation shows that, the first case of HAT in the country was reported in Maswa district (Mara region) in 1922. Since then endemicity has been reported in nine regions of mainland Tanzania. Like in many other countries of sub-Saharan Africa, the disease was successfully controlled in the 1960s, but made a dramatic re-emergence in the late 1980s. Little has been done in terms of management of the disease over the past decade. This is due to limited resources available for the control of HAT. Effective control options for HAT are mainly based on medical surveillance, consisting of early case detection and treatment, vector control as well as treatment of reservoir hosts.

Tanzania is currently affected only by *T. b. rhodesiense*, 4-5 million people are at risk of infection and only 1% of the population is under any regular surveillance (Komba *et al.*, 1997). The disease occurs in nine endemic regions of mainland Tanzania, namely Kigoma, Tabora, Rukwa, Mbeya, Arusha, Manyara, Lindi, Ruvuma, and Kagera (NIMR 2002). The estimated annual average is 264 cases, although this figure may not represent the true magnitude of the disease burden in the country due to poor diagnostic capacity and also disease under-reporting (Kibona *et al.*, 2002). Over the past 40 years, the number of new cases reported annually has rarely risen above 500. However, despite the endemic nature of the disease, occasional upsurges into epidemics proportional to socio-ecological changes in the infested areas have also been reported (Kibona 2001). Figure 1.3 shows the disease distribution across Tanzania.

Figure 1.3 Regional distribution of sleeping sickness in Tanzania



In Tanzania, however, control of human African trypanosomiasis has been complicated by a number of factors, including inadequate surveillance and other control activities. There are only few health facilities with the capacity to diagnose and treat the disease in most of the disease endemic villages. Moreover, poor infrastructure leads to poor accessibility to centres with the capacity to diagnose and treat the disease. Another important factor is the migration of people from disease endemic areas to non endemic areas; the aim of their migration being to explore good pasture for farming and their herds. There is also an increase in human activities and settlement in reserve areas looking for the fertile land.

Surveillance and control activities have been concentrated to the western parts of the country mainly in Kigoma and Tabora and Rukwa region, which are considered to be high transmission foci (Kibona *et al.*, 2002).

Some of the control measures have been noted in the northern areas of the country, particularly in the main transport routes of Serengeti National Park (SENAPA), which since colonial times have been known to be low endemic foci for the disease. The park authorities have discouraged any kind of tsetse control activities inside SENAPA. Despite having severe tsetse infestation in most parts of the park, park authorities prevent any activity which involve killing of tsetse as they consider tsetse to be an important part of ecosystem (Mlengeya, 2001).

Recent records shows that cases of HAT still exist in some of the old foci of Tanzania, and also some silent foci are reporting re-emergence, moreover there have been reports of several cases of HAT amongst tourists returning home from tour trips in Serengeti National Park in 2000/2001 (Kibona 2001; Mlengeya, 2001). This has increased concern at both National and International levels taking into account the importance of SENAPA as an important tourist destination with more than 90,000 tourists visiting the park every year (TANAPA, 2002). Fortunately efforts to put the condition under control were successful using insecticide impregnated targets (IIT) in selected areas, although the maintenance costs in the National Parks has proved to be expensive due to high rates of destruction of the targets by wild animals particularly elephants, rhinoceros and baboons. (TANAPA, 2004)

There have been several publications from Tanzania on the association between sleeping sickness infection and wildlife populations.

Some of the research includes; the study to investigate an outbreak of human trypanosomiasis in Mwanza district, Tanganyika territory (Davey, 1924), while Moloo (1974) conducted a survey in Musoma district on the role of the vector in the transmission of Rhodesian sleeping sickness.

Following recrudescence of HAT in 1964 and an increase of annual incidences in SENAPA, concerns were raised as the region had been declared free and was developing as an important tourist destination. A large-scale survey on human African trypanosomiasis was conducted mainly in SENAPA and Ikoma Game Reserve and several villages of the neighbourhood of these sanctuaries (Geigy, 1971; Moloo *et al.*, 1971; Onyango and Woo, 1971). Findings from these studies revealed that 10% of the 115 wild animals sampled were infected with *T. brucei* sub-species. In a follow up study conducted two years later, Geigy and Kauffmann (1973) isolated further *T. brucei* subgroup strains. A more recent study conducted in the same area revealed that out of 220 samples from 15 different wildlife species, both warthogs and cattle were positive for human infective sub-species (Kaare *et al.*, 2002) .

In summary, HAT appears to be a disease of major socio-economic and public health importance in rural communities, where more than four million people are at risk. The disease is endemic in nine regions of mainland Tanzania. Between 1996 and 2004, 2460 cases of HAT were reported with over 95% of cases reported from only three regions of the Western zone, Moreover several relapses have been reported after drug treatment, and there have been no studies to determine whether both forms of HAT co-exist in Tanzania particularly in areas where refugees from DRC have settled. In addition and in common with other neglected diseases, there is paucity of good quality data on the burden imposed by the disease and the risk factors associated with infection. This thesis attempts to address some of these issues by conducting targeted field studies in affected areas as follows:

1.9 Objectives

The objectives of this thesis are divided as follows: Chapter II reviews the historical data of HAT in Tanzania since the disease was first recorded more than 80 years ago, with the aim of attempting to find the evidence of Gambian sleeping sickness in Tanzania and also to try to establish when exactly sleeping sickness occurred for the first time in Tanzania.

Chapter III, uses established methodology (Odiit *et al.*, 2005) to investigate the level of Rhodesian sleeping sickness under-reporting in disease endemic areas of Tanzania.

Chapter IV uses the findings from Chapter III to recalibrate the quantification of burden of Rhodesian sleeping sickness in Tanzania, using DALYs, as a measure.

Chapter V investigates the risk factors for *rhodesiense* sleeping sickness in Urambo, Tanzania through a matched case-control study, both at the village and within the village scales.

Chapter VI: summarizes the conclusions which can be drawn from the findings of this thesis and proposes the way forward towards further studies and options for control of HAT in Tanzania.

CHAPTER TWO:
HISTORICAL PATTERNS OF SLEEPING SICKNESS IN
TANZANIA

2.1 Background Information

Descriptions of human African trypanosomiasis (HAT) or sleeping sickness is have been made since before 1700. In the literature, the first descriptions were made by European colonists in the late 16th and early 17th centuries. In 1742, the English naval surgeon John Atkins (1665-1757) described the disease as a “sleepy distemper” (Ormerod, 1961), while in 1792, Thomas Winterbottom who was a Physician to the Sierra Leone Colony found a disease and described it as “negro lethargy”. It was described that slaves who presented with swelling of the posterior lymph nodes (which is associated with African trypanosomiasis) were rejected by their shippers. In 1857, David Livingston (1813-1859) described it as a “fly disease” (Vickerman, 1997). Livingston recorded that a significant proportion of the cattle he carried along Limpopo valley, Zambezi River and at the banks of the Lakes Nyasa and Tanganyika died after they had been bitten by tsetse flies (Buxton, 1948). In east Africa, the disease has been confined to specific areas (foci), and many epidemics have ravaged these foci during recorded history starting 1900 onwards (Hide, 1999). The first recorded major epidemic of sleeping sickness was the Busoga focus in Uganda where *T. b. gambiense* was thought to be the causative agent of the disease, although at that time the more familiar East Africa subspecies, *T. b. rhodesiense* had yet to be described.

2.1.1 Evidence of First Sleeping Sickness Appearance in Tanganyika (Tanzania)

Although available documentation suggest that sleeping sickness was first recorded in the Tanganyika Territory (now Tanzania) in 1922. Considerable debate about this still goes on about when exactly sleeping sickness appeared in Tanzania; there is possibility that the disease may have been present even before 1900. In tracing the origin of the human trypanosomiasis outbreak in Mwanza district, Davey (1924) wrote that a blood film from a case which died in Mwanga native hospital examined in 1919, confirmed a heavy trypanosome infection, it is improbable that this was the first case.

He suggested that the disease had been endemic in Usmao sultanate (Maswa) for several years. According to Davey (1924), a considerable number of sleeping sickness cases escaped detection within fifty miles of a medical station for four years. At the moment *T. b. rhodesiense* is still present in western regions of Tanzania. The Rhodesian form of sleeping sickness is believed to have reached Tanzania from Zambezi river basin in Mozambique (then Portuguese East Africa) across Ruvuma river in 1910 (Fairbairn, 1948). Having gained a foothold in the South-east fly belt, involving Ruvuma, Mtwara, Lindi and Morogoro regions, the disease spread (by both riverine and woodland tsetse) northwards to the fly belt between Lakes Tanganyika and Victoria (Apted, 1970).

2.1.2 Evidence That Gambian Sleeping Sickness has occurred In Tanzania

Available documentation suggest that cases of Gambian sleeping sickness occurred in Tanganyika during the German rule, before 1914 (Buxton, 1948). From his illustration (*Med. Berichte deutschen Schutzgebiete* 1908, 1909), Buxton described that human sleeping sickness occurred along the whole extent of the shores of Lake Tanganyika, where *G. palpalis* was the predominant species. It is also believed that both *T. b. gambiense* and *T. b. rhodesiense* existed in the country in separate epidemics, the first being recorded at the turn of the eighteenth century (Buxton, 1948; Kihamia *et al.*, 1991). It is documented that *T. b. gambiense* spread from West Africa through Belgian Congo (now DRC) into Uganda and subsequently reached Bukoba and Shirati in 1902 (Mwaluko *et al.*, 1991). Fairbairn (1948) documented that, *T. b. gambiense* sleeping sickness reached German East Africa (now Tanzania) from Uganda in the early years of the last century. This situation prompted the Germans (then colonizing the Territory) to establish camps in Kigarama on the west shore of Lake Victoria and Shirati on the eastern side of the lake in 1907 (Fairbairn, 1948). Despite enquires by a German doctor (Dr. Feldmann) in 1903; natives of Ukerewe revealed that sleeping sickness was not new to the people.

In local vernacular people of Ukerewe named the disease *Ruti* and *Msiro* although there was no evidence of major epidemics in the area (Clyde, 1961).

However, Dr Feldmann who was then stationed in Bukoba revealed cases in migratory workers returning from Uganda (Kihamia *et al.*, 1991). The first autochthonous cases were reported in 1904 from Kome Island in Lake Victoria, an area which was infested with *Glossina palpalis* (now suggested to be *Glossina fuscipes fuscipes*). A second focus was found amongst villagers living along the North-eastern shores of Lake Tanganyika in Kigoma and Ujiji. On the eastern shores of Lake Tanganyika it is believed that *T. b. gambiense* was contracted across the shores of Lake Tanganyika from western shore of the Lake in the Belgian Congo (DRC) (Temu, 1981). The disease was rampant and the Germans, then colonizing Tanganyika, resorted to stringent control measures such as effective bush clearing and strict control of population movements. The disease was almost eradicated by 1914 (Temu, 1981). By the end of the First World War, only a few cases of sleeping sickness were found from small persistent foci near the Rwanda-Burundi frontier (Duggan, 1970).

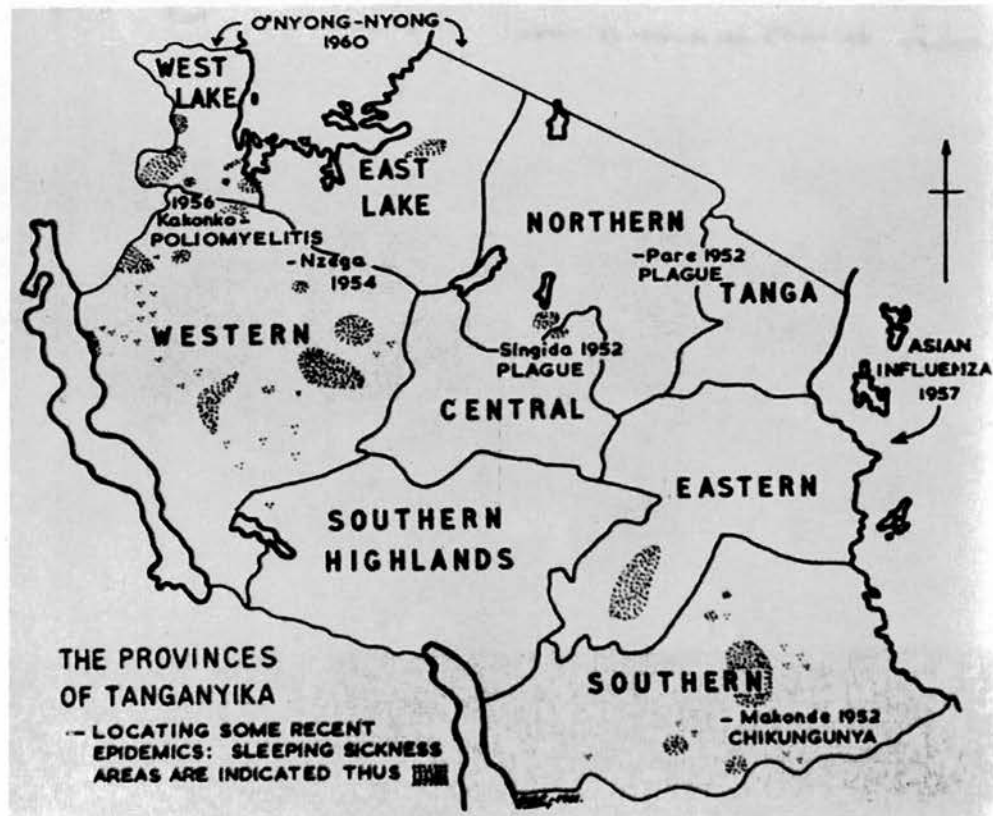
Gerald F. Sayers reported that, the first known case of sleeping sickness occurred in the territory in 1918, with no further cases until 1922 when a number of cases were found in the neighbourhood of Maswa (Sayers, 1930). A. J. Oliver, the then Western Region Regional Development Officer, in his 1962 report on tsetse survey and control for Lake Tanganyika, confirmed cases of Gambian sleeping sickness for the first time in 1924 (Oliver, 1962). Between 1924 and 1933, a fairly low but steady rate of infection was maintained (Temu, 1981), with none reported between 1934 and 1952. In 1953 a sudden outbreak occurred with 163 cases recorded (Oliver, 1962). This abated following intensive surveys, compounded with spraying campaigns, clearing of settlement boundaries and treatment of all cases. A total of 38 Gambian sleeping sickness cases were recorded in Kagunga (Kigoma) between 1957 and 1958, however, these are believed to be the last cases of Gambian sleeping sickness in Tanganyika (Oliver, 1962).

2.1.3 Patterns of Sleeping Sickness Distribution in Tanzania

In another debate, the spread of sleeping sickness from Mozambique to the southern part of the country arises from the shores of Lakes Tanganyika and Nyasa (Fairbairn, 1948). John Iliffe documented that sleeping sickness followed a decade or two behind 1914. It was confined to the upper Ruvuma valley and the shores of Lakes Victoria and Tanganyika, where several people contracted the disease during the war (Iliffe, 1979). He called sleeping sickness the “natural disaster” of the 1890s, and further explained that it was an “ecological catastrophe fundamental to Tanganyika 20th century history” (Iliffe, 1979). He also reported that the deserted fields quickly relapsed to bush, and were soon reinfested with tsetse flies. Cattle began to die of trypanosomiasis followed by appearance of the disease in men characterised by fever and lassitude followed by to coma and death. It has also been reported that as early as 1915, a number of deaths were characterized by the swelling of legs in the vicinity of the Mtäte River (Maclean, 1926). Dr. F.I.C.Apted documented that, sleeping sickness existed around Lake Ruvuma as early as 1911 from where it slowly diffused northwards through the eastern fly belt to involve the Eastern Province in the late 1920s (Apted, 1970). David Clyde (1962) documented that in August 1911 sleeping sickness crossed Rhodesia and Mozambique and broke out in a new area, the Ruvuma area near Songea (Clyde, 1962). He also wrote that, Prof Beck who was transferred to Lindi in 1908 to take the responsibility of Regional civil medical officer, spent much of his time investigating the spread of sleeping sickness down the Ruvuma river until his capture in 1916 (Clyde, 1962). However, according to the existing reports, the earliest foci appear to have existed in Maswa and Ufipa in Mara and Rukwa regions respectively, where severe epidemics were reported in the territory around 1920, or some years earlier. These foci involved the greater part of the Western province. As early as 1932, 11,000 cases of sleeping sickness had been reported, out of them 3000 cases reported in one year (1930), and more than 2,000 in a single district (Apted, 1970).

People who lived in the infected areas were dispersed far and wide due to fear of infection and subsequent death; the situation which Maclean (Maclean #428) called “stampede of population”. The disease spread rapidly northwards reaching Tabora by 1926 and Kahama by 1928. And as early as 1930 the disease had reached Mwanza from where it spread to Ukerewe Island in Lake Victoria by 1939 (Temu, 1981). It also spread westwards to Kigoma and West Lake. According to the reports, severe outbreaks in West lake which involved Ngara district occurred in 1954 (Temu, 1981). If we group the epidemiological distribution of sleeping sickness in Tanzania regionally since it was first recorded, then endemicity has been reported in seventeen regions of mainland Tanzania, which include: Arusha, Lindi, Ruvuma, Kagera, Kigoma, Tabora, Mbeya, Rukwa, Mwanza, Shinyanga, Kilimanjaro, Morogoro, Iringa, Dodoma, Singida, Cost and Mara. Figure 2.1 shows the colonial map of Tanganyika incorporating provinces as well as the location of sleeping sickness foci.

Figure 2.1 Map of Tanganyika Territory showing different epidemics of different diseases and foci of sleeping sickness (Clyde, 1962)

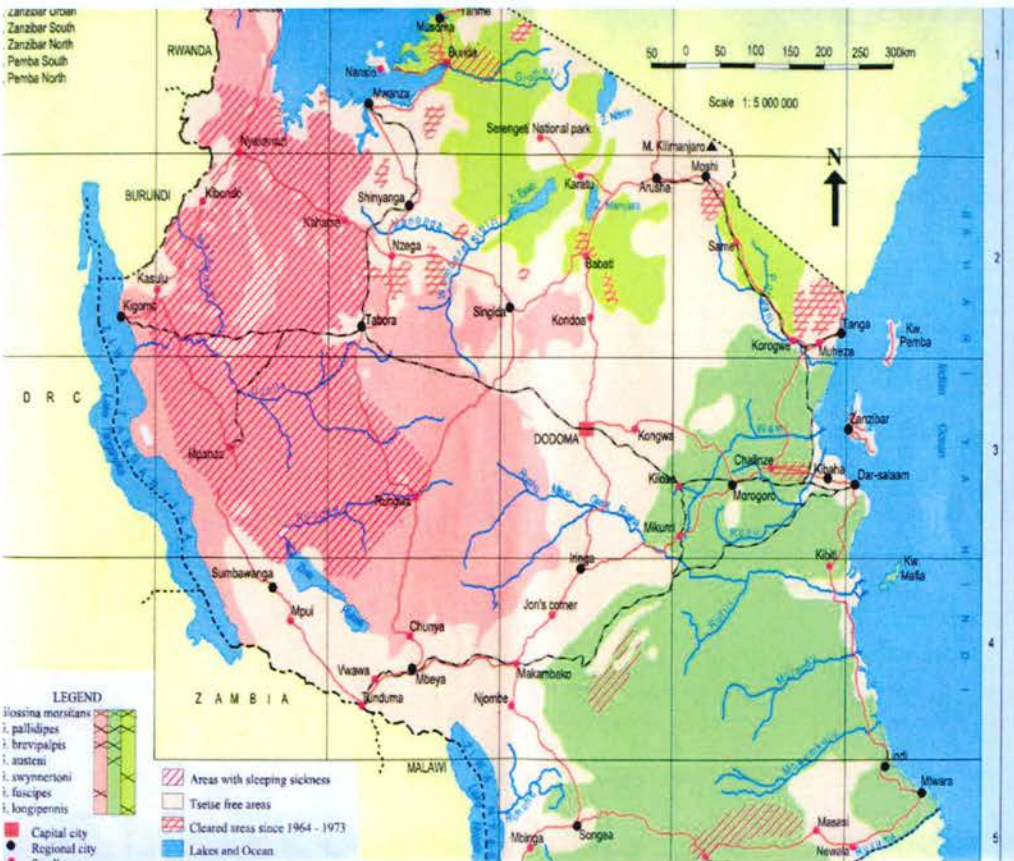


Map of Tanganyika showing Provinces (renamed Regions in 1962).

2.1.4 Tsetse Distribution in Tanzania

Historically, seven species of *Glossina* are of economic importance in Tanzania, transmitting infection to both human and livestock. In order of importance, these are *Glossina morsitans*, *Glossina pallidipes*, *Glossina swynnertoni*, *Glossina brevipalpis*, *Glossina austeni*, *G. f. fuscipes*) and *Glossina longipennis* (Daffa *et al.*, 2005). These were distributed as follows although overlaps of species have existed in many areas (Fairbairn, 1948); *G. morsitans* was the predominant species observed mainly in the Western and Eastern blocks with pockets of both *G. pallidipes* and *G. brevipalpis* also occurring in the same areas. The northern fly block was the main habitat for *G. swynnertoni*, and *G. pallidipes* which was also widespread throughout the area *G. brevipalpis* was only observed in few isolated areas. The shore of Lakes Victoria and Tanganyika were the main habitat for *G. f. fuscipes*. However, *G. morsitans* has also been reported to have invaded Lake Tanganyika shores from Malagarasi delta. The regions bordering Kenya extending to Mbulu district were preferred by *G. longipennis*. North east and along the coast including the island of Zanzibar were the main habitat for *G. austeni*. However, there were few areas where the overlap of *G. morsitans* and *G. swynnertoni* was observed, including Shinyanga (Mwanza Province) and Babati (Northern Province). There have been desirable efforts in an attempt to reduce the abundance of tsetse flies in Tanzania. However, very little eradication has been achieved and to date all the listed species of tsetse fly still exist in various areas of Tanzania. Figure 2.2 shows tsetse distribution in Tanzania.

Figure 2.2 Map showing the distribution of tsetse in different areas Tanzania (Ford and Katondo, 1977). According to sub-generic group scale of 1:5,000,000



About 50% of rangeland in use in Tanzania is tsetse infested, exposing four million people and seven million cattle at risk of trypanosomiasis (Daffa *et al.*, 2005) These tsetse flies have denied livestock a large portion of good grazing land due to animal trypanosomosis, leading to problems of over-grazing and soil degradation of tsetse free lands.

2.1.5 Methods Used for Control of Sleeping Sickness in Tanzania

Over the past 80 years, various control methods have been applied in Tanzania, often in combination. These measures have been categorized by Temu (1981) into four groups as follows: a) system of notification of cases, b) control of man-fly contact, c) vector control and d) the control of animal reservoirs.

In the system notification, all cases diagnosed in any of Tanzania districts, were filled onto a notification card and sent to the sleeping sickness unit in Tabora (now National Institute for Medical Research) which was then the sleeping sickness headquarters. In line with this system, existed the so called “Pass Card System” in the east African Territories whereby all people were examined before they were allowed to travel; the pass was obtained from the chief and it was countersigned by a “gland boy” after thorough examination of the holder to ensure the latter was not suffering from sleeping sickness (Granville Edge, 1938). In situations where a positive finding was recorded, the chief was informed and the person concerned was either sent to the nearest treatment post or detained to be treated by the itinerant orderly who visited these centers once every week (Granville Edge, 1938).

In the control of man-fly contact; there was a creation of fly-barriers between settlements and tsetse bush. Through awareness creation and massive educational campaigns to people in the risk areas as well as drawing attention that should incidental biting occur, they were obliged to report any febrile conditions occurring following the visit to tsetse areas for appropriate medical check-ups.

The most dominant measure of all the control methods used was the vector control and was sub divided into four sub-groups as follows:

- i) Hand catching – this is probably the most ancient pest control method. It was effective in the species which are attracted to man such as *G. palpalis* (Glasgow, 1970).

- ii) It also involved the use of traps and bait animals so as to enhance the fly catch, this method was usually carried out by the so called “fly-boys” using hand nets on “fly rounds”.

- ii) Bush clearing may be partial or total - The method was first employed in Shinyanga by Swinnerton (1925) and following successes observed, it was advocated to be adapted to other areas of Tanzania with substantial tsetse densities.

- iii) The use of insecticides – This method was extensively used (Brun *et al.*, 2001) and involves application of residual insecticides on breeding sites on the ground, and aerosol applied over wide tsetse habitats by aircrafts. Much of the insecticide control work was conducted by the Tropical Pesticide Research Institute (TPRI) Arusha. A good example of this is the control of sleeping sickness in the Lossitete Forest (Tarimo, 1973)

- iv) Sterile Insect Technique -. It involves the release of gamma sterilized male flies into the environment to compete with the wild males in mating (Vreysen *et al.*, 2000). This method has been explained in detail in chapter one and it proved successful in Zanzibar where *G. austeni* males sterilized by gamma irradiation were dispersed by air over the whole island in 1994. As a result, Zanzibar has been free from *G.austeni* since September 1997 (Saleh *et al.*, 1998). However this method encountered several difficulties including the enormous costs of implementation and low density of target population required for the SIT to be effective (Politzar, 1982).

Finally the control of animal reservoirs which basically focused on game destruction – experimental game destruction which was conducted in Shinyanga between 1945-1954 (Potts, 1952). This method was not favored and did not receive acceptance in Tanzania for several reasons. First; in areas where game destruction experiments were conducted, flies were constantly driven to feed on man owing to scarcity of game (Davey, 1924).

Second, tsetse abundance was not reduced despite considerable number of animals killed by shooting as well as driven in small detached belts of *G. morsitans* (Jackson, 1939).

Despite all control measures detailed above that have been applied in Tanzania, little has changed in terms of tsetse fly distribution and in fact, the distribution may have even extended (MacLennan, 1980). Clearing of vegetation and the destruction of wild animals were widely practiced in the past. These methods have been shown to be inefficient and are not popular today for environmental and conservation reasons.

Regression of the tsetse fly has occurred in areas where pasture development and land cultivation have taken place. Almost all tsetse control methods in use to date involve the use of insecticides (Tsetse report, 1960), through spraying or dipping livestock, as well as the use of insecticide impregnated targets. The methods explained earlier such as aerial spraying are, however, expensive and their wide use in Tanzania has been limited by the scarcity of funds. Extensive areas of western Lake Region (now Kagera) were successfully sprayed in the past although tsetse flies are now reported to be re-invading the area (Temu, 1981). Tsetse traps and insecticides impregnated targets constitute a recent development that could prove practical and useful in Tanzania. There exists a paucity of information about when exactly sleeping sickness was recorded in Tanzania and also it is unclear whether Gambian sleeping sickness ever existed in Tanzania. In realizing this all available documentation were reviewed and analyzed for the purpose attempting to fill the existing gap.

2.2 Objective

The aim of the study detailed in this chapter is to review the historical patterns of sleeping sickness in Tanzania for both Rhodesian and Gambian forms.

2.3 Material and Methods

The National Institute for Medical Research (NIMR) Tabora Centre was established in 1922 as a sleeping sickness unit and was mandated to carry out trypanosomiasis medical surveillance, treatment of cases and follow up of all treated patients and also liaison with tsetse control staff. Tabora is located about 1000 Km west of the capital Dar es Salaam. The author therefore visited and reviewed all historical records located at the archives at the NIMR Tabora, Tabora Regional Hospital (Kitete), Kibondo District Hospital, Kasulu District Hospital, Kabanga Missionary Hospital and Heri Mission Health Centre in Kasulu (Kigoma).

The author investigated all available hospital reports, sleeping sickness patients data including patients case notes, annual reports and all other documentation regarding sleeping sickness since the disease was first reported in Tanzania (then Tanganyika) more than 86 years ago.

2.3.1 Differentiation of *T. b. rhodesiense* from *T. b. gambiense*

There are several possible approaches to differentiate *T. b. rhodesiense* from *T. b. gambiense* from archival samples and records; the first is the use of molecular techniques, which requires availability of genetic materials from the patients, which can be in the form of stored samples or historical slides (Picozzi *et al.*, 2005; Radwanska and Chamekh, 2002; Welburn *et al.*, 2001a). Second is the use of statistical methods to analyze the archival records. There are very limited sleeping sickness studies, where such methodologies have been demonstrated. One of them is the study conducted by Dr. M. Odiit in Tororo in 1997, where he used the duration of symptoms of patients, who died from Rhodesian sleeping sickness within a week of seeking treatment in LIRI Hospital in Tororo (Odiit *et al.*, 1997).

In a separate study Dr. E. M. Fèvre in 2004, reanalysed the 1900 – 1920 sleeping sickness epidemic using survival analysis of the clinical course of illness from first onset to distinguish the two forms of the disease; the results obtained enabled the suggestion of the possible organisms responsible for the 1901-1920 epidemics in Uganda (Robays *et al.*, 2007). Since it was not possible to obtain such archival genetic patient materials, which would have provided an easier option to address the question of the possible existence of Gambian sleeping sickness in Tanzania, the current review therefore analyses available historical data using statistical methods.

2.3.2 Archival Records

Existing documentation suggests that sleeping sickness may have been present in Tanzania before World War I (WWI)(Clyde, 1961).

However, due to poor storage programmes in hospital archives which lack proper storage of documentation such as old hospital reports, patient case notes (which are destroyed every ten years), or monthly returns, though it may seem that available records are not enough evidence to support the possibility of Gambian sleeping sickness existence in Tanzania, however, unless proved otherwise all documented evidence has to be reported. The only records available are for the first outbreak of sleeping sickness from 1920s onwards; these were in different forms varying from annual reports, patient monthly/annual returns, maps and research reports findings. In most hospitals visited, all patients' records particularly patient case notes, and files are destroyed after every 10-15 years for lack of storage space in the hospital archives.

In the past, sleeping sickness wards at Tabora Regional Hospital were managed by the National Institute for Medical Research, Tabora. Currently all NIMR clinical staff have moved from the regional hospital to NIMR premises. Some old patient files and most of old information related to sleeping sickness patients were left in the hospital archives as the former sleeping sickness wards (initially under NIMR) have been taken over by the hospital. However, NIMR continue providing clinical expertise and consultation to all sleeping sickness patients diagnosed at the regional hospital and referrals from endemic districts. In the past, whenever a case of sleeping sickness was diagnosed in any district, the requisite information was filled in a notification card and forwarded to the sleeping sickness Headquarters (NIMR–Tabora) as detailed in section 2.1.5 above. Therefore all archival documents available at NIMR (Figure 2.3) as well as visited hospitals were reviewed.

These include hospital registers monthly and annual returns, patient notes as well as documented communication details related to sleeping sickness in the visited centres. All the available findings were compiled and analyzed.

Figure 2.3: Old record shelves at National Institute for Medical Research Tabora archives



2.3.3 Data Management and Analysis

All available documentation was reviewed and analysed using graphical methods, data obtained from the review was compiled, summarized and analyzed in (Microsoft Excel®, 2003). Respective graphs were plotted; temporal and epidemic trends from first recording were produced and are reported in the results section. These are based on the assessment of temporal patterns and distribution of sleeping sickness in Tanzania

2.4 Results

Analysis of historical data revealed very high epidemic peaks in the late 1920s and early 1930s (Figure 2.4), which denotes the period of great depression which followed immediately after the WWI, shown as Section A on the graph in Figure 2.4.

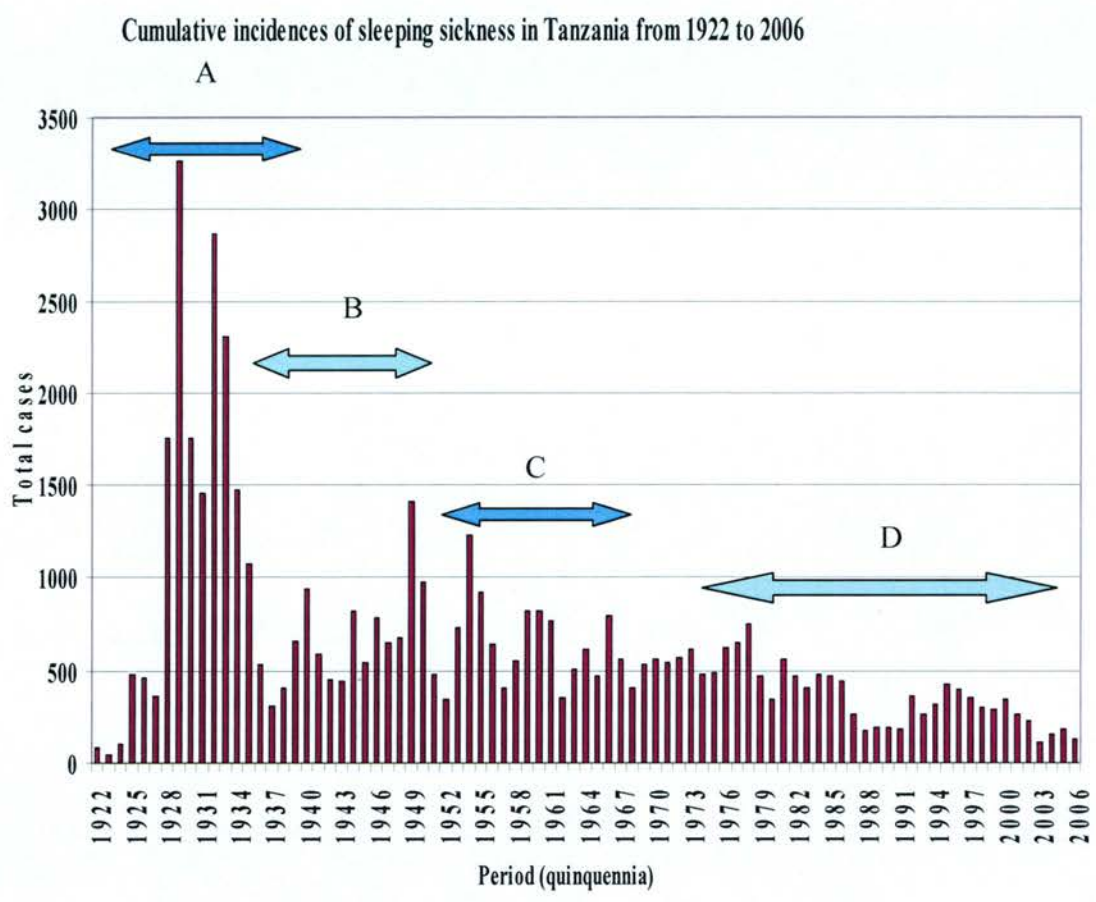
The epidemic maintained a high rise trend which lasted until 1935, when a significant decline was observed. The subsequent decline was observed across most of the highly endemic districts of western Tanzania (section B). This denotes the period of the World War II (WWII), this lasted until 1948 when the rise was observed again.

There are several suggestions that can be associated with this decline and they are discussed later on in this chapter (section 2.5). This high rise which was immediately followed by decline (shown as section C in Fig 2.4), and a slight rise was not stable and kept fluctuating until 1960 when another decline was observed. Most of these cases were recorded along the shores of Lakes Victoria and Tanganyika (Kilama, 1981; Temu, 1981)

This review also shows that the highest records of sleeping sickness were recorded from the only few districts of western Tanzania. The cumulative data (Figure 2.4) also shows that few epidemics occurred during this period. The first epidemics lasted for 11 years starting from 1925 to 1936, during this epidemic, 17,772 cases were recorded (NIMR Archives).

During the decline period which started from 1937 and ended around 1949, a total number of 8765 sleeping sickness cases were recorded. This was followed by a slight rise lasting for about ten years when 8712 cases were recorded. The final period (section D) shown on the Figure 2.4 which started in 1961 to 1986, was not much different from the decline period comprising of 13,938 cases. Figure 2.4 below is a cumulative incidence graph showing all the sections described.

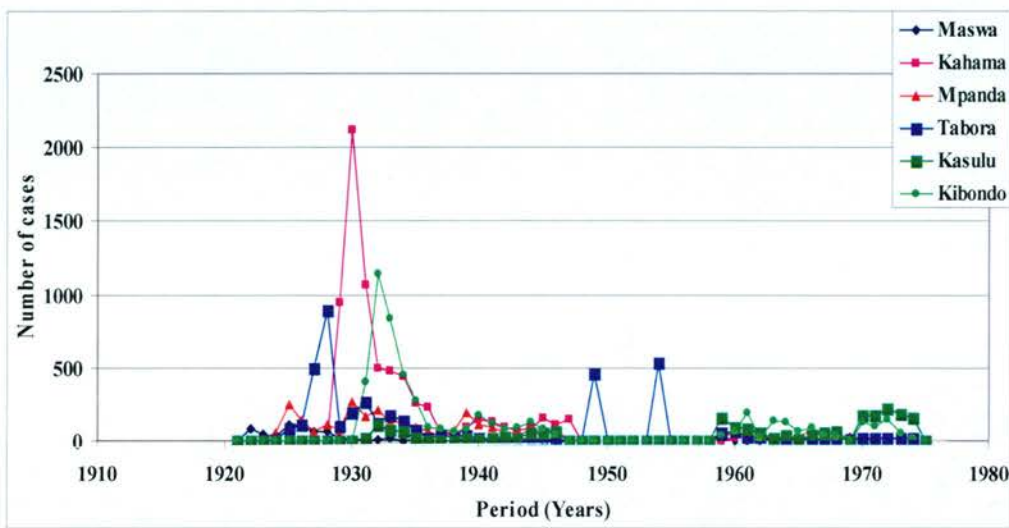
Figure 2.4 **Graph of incidences of sleeping sickness cases in Tanzania from 1922 & 2006**



A, B, C and D are suggested epidemic peaks

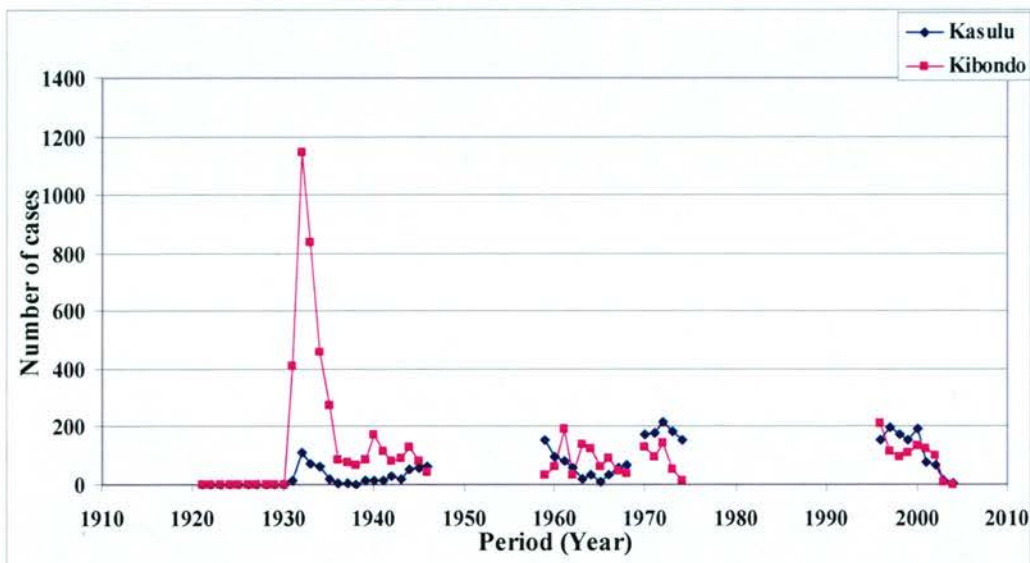
To allow clear observation of the actual situation in the districts, this chapter carried out a review and analysis of all available data of sleeping sickness since the disease was first recorded in 1922 until 1980. The annual incidence are plotted separately in Figure 2.5. The comparisons of temporal trends of sleeping sickness between neighbouring districts are plotted separately in Figures 2.6 to 2.8.

Figure 2.5 **Graph showing cumulative incidences for the six most affected districts.**



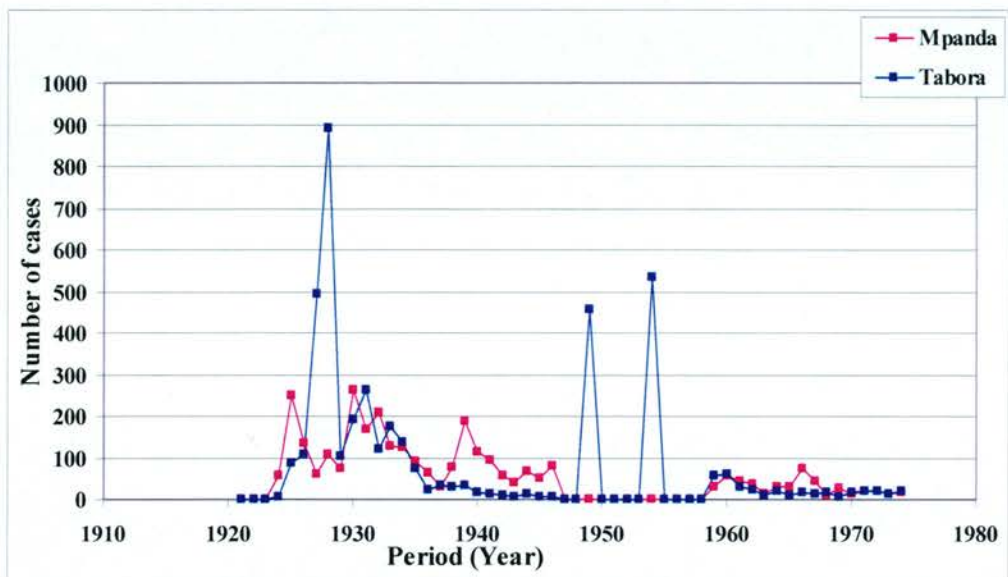
The graphs (Figure 2.5) compare temporal trends in different districts of the western part of Tanzania in different years. In the graph shown in Figure 2.5, high rise peaks are observed across four out of the six districts (Kahama, Kibondo, Tabora and Mpanda) between mid 1920s and mid 1930s. However, there was a subsequent decline observed from late 1930s followed by a slight increase in two out of the six districts (Kahama, Maswa, Kibondo, Kasulu, Mpanda and Tabora) observed around 1940s, extending to 1949. There was another peak observed in Tabora between 1949 and 1956. In the graph also it is observed that there are small peaks between late 1950s and mid 1970s in Kasulu and Kibondo districts. To allow a clear picture of this small peak the two districts are plotted separately in Figure 2.6.

Figure 2.6 **Sleeping sickness incidences from 1922 – 1958 in Kasulu and Kibondo districts**



It is observed that Kibondo district recorded a high rise peak in number of sleeping sickness cases which started in 1931 and lasted for four years until 1938, as compared to Kasulu which recorded a moderate rise around the same years. There was another small peak starting from 1939 lasting to 1946, followed by subsequent decline across both districts. It's interesting to note that there was an unusual uniform several small peaks in the two districts between 1958 to 1968, 1970 and 1974 and also the last one observed in 1996 and ended in 2004. Figure 2.7 compares the trends in the Mpanda and Tabora.

Figure 2.7 **Graph showing incidence in Mpanda and Tabora district between 1926 & 1975**

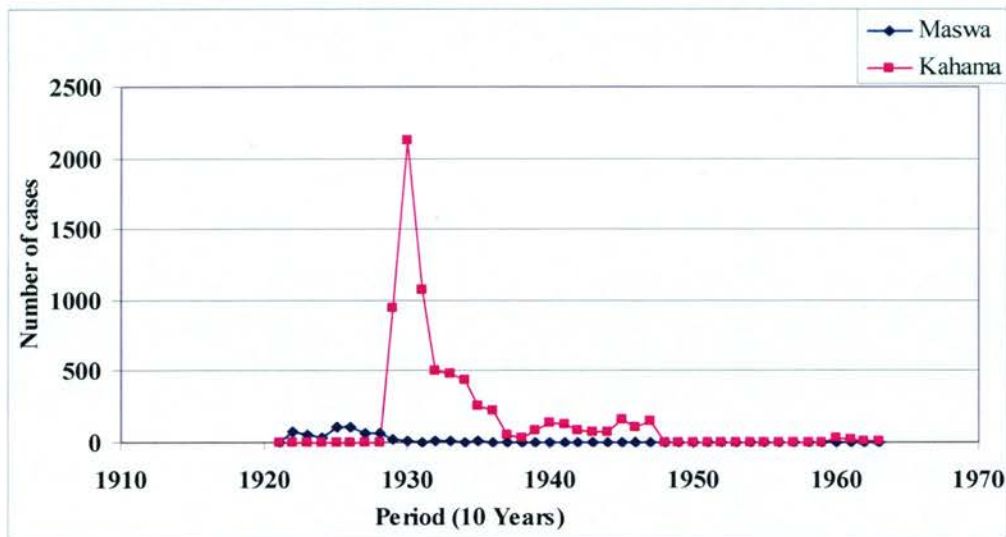


From the graph it is observed that Tabora district recorded the highest peaks which started in 1929 and lasted until 1934. This was followed by a decline lasting for about 15 years until 1949. In 1949 and 1954 two peaks were recorded and each lasted for just one year. From 1959 to 1974 both districts maintained low pace of incidences the highest number being 76 cases in 1966. On the other hand Mpanda observed moderate peaks in 1925, 1930, 1939/1941 and finally the one of 1966.

The review demonstrated that despite Maswa and Kahama being amongst the districts which recorded the first cases in Tanganyika territory, they also recorded the highest ever recorded peak in the territory. An outbreak was recorded in Maswa for the first time in 1922 and maintained moderate incidence until 1935 when the disease disappeared from the district. However, during this low records duration, the disease then entered Kahama district, which shares border with Maswa, in 1929 when annual incidence reached 948 cases. The following year 1930 the highest ever peak observed in the country when annual incidence for one district (Kahama) reached 2121 cases.

This was followed immediately by subsequent decline observed the following year, it continued to decline and by 1938 the annual incidence reached 50 cases (Figure 2.8).

Figure 2.8 The graph showing the incidences reported from Maswa and Kahama districts.



The findings from the review of existing records also show that there were few Gambian cases recorded from the shores of Lake Tanganyika. The documented records show that Gambian sleeping sickness was first recorded in 1924. Figure 2.9 is the graph showing incidence of Gambian sleeping sickness in the territory and Figure 2.10 is the map of Tanganyika showing the exact location of Gambian sleeping sickness.

The results described from the archive reports suggest that both Rhodesian and Gambian sleeping sickness have existed in Tanzania. Fairbairn documented that the possible occurrence of Gambian type of disease, on the eastern and southern shores of Lake Tanganyika needed to be discussed (Fairbairn, 1948). It was known since German colony times that human sleeping sickness occurs along the whole extent of that shore habited by *G. f. fucipes*. However, subsequent entomological studies conducted along Lake Tanganyika shores shows that *G. morsitans* and *G. palidipes*, exist in the same areas and an outbreak reported in 1943 was found to be due to *T. b. rhodesiense* (Fairbairn, 1948).

Findings from the current review analysis demonstrated a high epidemic peak which started around the 1920s and lasted for about ten years, the observed rise was likely associated with a number of things, first was a period of great depression following the WWI, secondly the transition from Germany colony to British mandate. Most of the control programmes which were under German authority were left without funding and proper supervision as most of the programmes were manned by European experts, David F. Clyde (1962) wrote that, owing to shortage of medical officers in the years immediatly following the war the disease was not reported (Clyde, 1962). It is therefore possible that the high rise trends observed were due to the stability in number of medical staff recruited after the power take over from the German administration.

The decline observed after the beginning of the 1930s is the result of combination of issues, which can be suggested to contribute towards this achievement. Amongst the most important ones again being the improvement in numbers of the medical staff who facilitated the diagnosis and treatment (Clyde, 1962). Second, was probably the introduction of a new effective drug (Suramin) for the treatment of sleeping sickness in Tanganyika (Duggan, 1970).

And third there were large scale mass bush clearing campaigns around the villages and along the roads, at least 150 yards on each side of the road (Swynnerton, 1924), the impact which can be observed until today. Local residents of Kahama and Shinyanga, the districts which were involved in these campaigns believe that the semi-desert feature observed in most of these areas today is the result of the campaigns (personal communication). Kahama is among the districts which recorded the highest sleeping sickness numbers in the past. However, the last four cases were diagnosed in 1972 and since then no new cases have been diagnosed in the district.

In 1919 it was reported that, while epidemics prevailed in the Congo basins, sporadic cases of the virulent form of trypanosomiasis were reported from Tanganyika (Duggan, 1970). The virulent kind of unusual trypanosomiasis mentioned by Duggan suggests that this was Rhodesian sleeping sickness. It is also documented that the mentioned virulent trypanosomiasis was transmitted by riverine tsetse flies. This raises concern since Rhodesian sleeping sickness is rarely transmitted by this species of tsetse. However, later studies suggested that both species of tsetse flies existed in the region

It may be argued that, available data does not provide enough evidence for the existence of gambiense sleeping sickness in Tanzania. Also considering diagnostic facilities which were available in the past which relied on microscopy, there is probably not enough evidence to support the existence of *T. b. gambiense*. When comparing the two forms of the disease, clinically Rhodesian sleeping sickness is more acute than Gambian (Apted, 1970). Beside, records show that there were more cases of *T. b. rhodesiense* (23,955 cases between 1922 and 1946) as compared with *T. b. gambiense* which totalled an annual incidence that hardly reached 170 since it was first recorded in 1924. It is not clear and not documented anywhere how these cases were diagnosed or even how they were differentiated from Rhodesian HAT cases.

When looking at the kind of control measures which existed between 1920 and 1958, which included intensive bush clearings, settlement in new areas, treatment of cases and vector spraying. Apart from all these measures, an officer was sent to a gambiense focus in Kenya to acquire experience and skills of controlling gambiense form of the disease, it is, however, unclear why there was so much attention given to the focus with such small number of cases along the shores of Lake Tanganyika to eradicate *G. palpalis* as compared to other areas in the same province where large number of cases were reported. The only possibility is that, the authorities were trying to avoid serious consequences which were likely to occur if the disease was allowed to develop further and cause an overlap to *rhodesiense* sleeping sickness which was already widespread.

It was documented that in East Africa existed "A Pass System" (Granville Edge, 1938) for the control of population movements across the borders. This reduced the chance of introducing the disease to the other side of the border. Although chances still exist for the people who contacted the disease and travelled before parasite could be demonstrated in their blood. In the Annual report for the tsetse survey and reclamation for 1958, it was reported that there was a massive spraying campaign between Kigoma and Ruanda - Burundi border (Annual-report., 1959). Beside there was another re-spraying operation in some parts of the river where few flies persisted, such that by December 1958 not a single *G. palpalis* was found in Kigoma (Annual-report., 1959). In the veterinary report from 1959 they reported that the surveys conducted shows that, although eradication campaigns were still on, traces of *G. palpalis* were reported particularly in the southern parts of the lake shores. But still no cases of *T. b. gambiense* were found. The two reports contradict each other and it is possible that one of the groups which conducted the survey was probably not accurate enough, as it is unlikely that there would of been re-invasion just one year following eradication.

Beside, presence of *G. palpalis* group does not always warrant the existence of gambiense sleeping sickness as research findings shows that *G. palpalis* (*G. f. fuscipes*) also transmit Rhodesian sleeping sickness (Southon and Robertson, 1961; Willett, 1965).

Sleeping sickness epidemics were controlled in some parts of Tanzania before 1960s using conventional methods which included bush clearing; large scale spraying campaigns, mass diagnosis and treatment of cases. In Uganda for example political and economical upheaval has been associated with the resurgence of disease epidemics in the country (Mbulamberi, 1989a). In addition a number of factors and hypothesis have been advanced as possible cause of the outbreaks of sleeping sickness which occurred in Uganda at the beginning of the 20th century which were attributed to *T. gambiense* (Mbulamberi, 1989a). However, reanalysis conducted later to old patients documentation suggested that probably rhodesiense HAT was responsible for the outbreaks (Odiit *et al.*, 2004) It is very possible that similar confusion exist in available documentation. In Tanzania on the other hand no *T. b. gambiense* epidemic has ever been reported, moreover the overall annual total of *T. b. gambiense* cases in the country hardly reached 170. The re-invasion of *G. palpalis* group was reported in areas where previously controlled (Report, 1960; Officer, 1960). This gives an interval of only one year after the area was declared free from the *Palpalis* group. It seems, however, unlikely that the disease could have disappeared so suddenly particularly in areas with reported re-invasion, if we assume both reports are correct. Considering that, gambiense sleeping sickness is chronic in nature, meaning that an individual may harbour the disease for several months or even years without developing any symptoms (Apted, 1970). Diagnosis has always been difficult particularly in the past, when the only means of diagnosis was purely parasitological. Moreover, parasitaemia in Gambian form is usually lower when compared to Rhodesian HAT.

This may have provided chances for the disease to maintain itself and spread even to other areas since no treatment would have been given, due to late diagnosis.

If it is assumed that the failure to find cases during those years was probably due to disease under-detection, it however, becomes difficult to explain why no single case of gambiense has been diagnosed in Tanzania since 1958. There is a risk that the disease may re-appear at any time since there no evidence of sufficient surveillance activities particularly in the old gambiense foci.

There is very limited documentation of similar control achievements with gambiense sleeping sickness endemic areas in sub-Saharan Africa, even in areas with better surveillance systems, with the use of mobile teams in active case findings, and with the use of modern and sensitive diagnostic options such as serology (Magnus *et al.*, 1978) in field environment.

Similar confusions were reported in Busoga (Uganda) where gambiense sleeping sickness was initially thought to be behind the 1900 – 1920 epidemics until later studies (Fevre *et al.*, 2004) highlighted that *T. b. rhodesiense* was probably responsible for the outbreak. Although the possibility of *T. b. gambiense* existence in Tanzania in the past cannot be ruled out especially if it is assumed that the reported successes which managed to eradicate Gambian form of the disease, were probably due to massive control campaigns conducted in the region during the 1950s, then several questions remain unanswered. It is understood that the control campaigns were extensive and directed towards tsetse eradication in general and were not targeted towards eliminating a particular species of the fly. It does, however, become questionable how other species of tsetse flies managed to maintain themselves around the shores of Lake Tanganyika with such massive and extensive control interventions in the region (Brun *et al.*, 2001).

T. b. rhodesiense would have been probably the first to be eliminated in the region considering its virulence and acuteness feature which forces patients to seek medical attention. Also the higher parasitaemia levels in Rhodesian form make the disease easy to be diagnosed and treated hence better chances of disappearance.

Similar achievements have been documented in other districts of Tanzania where with the use of such massive control campaigns the Rhodesian form has not been reported (Tsetse report, 1935-1938; Tsetse report, 1940)

It was once speculated that sleeping sickness was introduced in Kigoma region by livestock transported by trains, as abundances of tsetse were observed to be carried by cattle in the trains. This means that rhodesiense sleeping sickness has long been present around Lake Tanganyika and with *T. b. rhodesiense* known to be a zoonotic disease (Hide, 1991; Maudlin *et al.*, 1990; Onyango *et al.*, 1966) could provide evidence for an animal reservoir. In most areas in the western part of the country, transmission occurs along the roads as well as railway lines. Today from personal observation this can also be confirmed as most of the affected villages are located along the transportation lines. A number of rhodesiense sleeping sickness cases are still present in some parts of Kigoma, and also the disease managed to maintain itself in the region since it was first diagnosed in 1920s. However, so far there is no single case reported from the gambiense focus at the shores of Lake Tanganyika.

During the historical data review, there was no enough documented materials of clinical evidence was found, which would have enabled analysis to be conducted to prove the existence of *T. b. gambiense* in Tanzania.

However, the following communication documents were found; letters between Dr. F.C.I. Apted and Dresser in charge of Kagunga dispensary (Figure 2.9), as well as communication between Michael Ashcroft from Tinde tsetse research to Dr. Apted (Figure 2.10). In the first letter Dr. Apted, who was then the medical officer in charge at Tabora Research Station and also the sleeping sickness specialist, was responding to the then in charge of Kagunga dispensary who was seeking advice on how to deal with cases of sleeping sickness which were not responding to treatment. Dr. Apted suggested a new line of management for these patients and also promised to send stock of drugs including Pentamidine to the dispensary.

Kagunga was reported to be one of the gambiense sleeping sickness focuses, and Pentamidine is known to be the drug of choice for early stage gambiense sleeping sickness. In the second letter they were arranging a visit to Kagunga to collect gambiense strains for the research purposes. While the author respects the outstanding clinical experience of these staff and since this may suggest some clues of gambiense, it is however unclear why Suramin which is the drug of choice for first stage *rhodesiense* sleeping sickness was stocked in a gambiense focus, if pentamidine was available.

Figure 2.11 Communication between Dr.F.I.C Apted and In charge of Kagunga dispensary

From:
W. I. C. Apted
27-11-56

Sleeping Sickness Specialist
Box No. 89 Tabora.

Sir

I have the honour to send you the Sleeping Sickness Report and monthly Return for February 56.

New Cases diagnosed this month Total 3 Cases.

I am just sending you the Sleeping Sickness Report for this month. As the first 2 cases Sleeping Sickness Cases are pointing to carry on sleeping all the time during the day. And some with 1/2 find negative 3 times of 1/2 find negative some have not yet but find negative and others they have not yet. I therefore ask what am I going to do with them?

Others will find fastest people. Usual are the Cases of 1953-54. So many people have complaints May, when people will come to give us information?

I hope my letter will meet you, Early.

I have the honour to be

Sir

Your Obedient Servant

W. I. C. Apted
W. I. C. Apted

SLEEPING SICKNESS OFFICE
P.O. Box 19
TABORA

216

SS/11/N/216 9th March, 56

The Dresser i/o,
Kagunga Dispensary,
KAGUNGA.

U.I.S. District Medical Officer,
Kigoma.

Thank you for your letter of the 29th February.

1). If a patient has not had treatment for sleeping sickness before but you think he has sleeping sickness now and you cannot find trypan in his glands or his blood then give him the usual treatment with antypol and tryparsamide. Call him a 'clinical case' in the monthly return.

2). If a patient has had treatment with tryparsamide but is now ill again or is sleeping such in the daytime do not give him more tryparsamide but give him five injections of Antypol. If he does not improve with the Antypol try to send him to Kigoma Hospital. Mark the disc numbers of all patients who have had Pentasidine on the monthly return forms.

4). Patients who have been treated for sleeping sickness before must not be included in the 'new cases' on the monthly return.

5). I shall come to give more Pentasidine injection at the end of July or the beginning of August.

FIGA/IS. F. I. C. Apted
SLEEPING SICKNESS SPECIALIST.

Figure 2.12 Communication between Michael Aschcroft and Dr.Apted arranging a visit to a gambiense focus Kagunga

SLEEPING SICKNESS OFFICE
P.O. Box 19
TABORA

SS/11/N/214

8th. March 56

EAST AFRICAN TRYPANOSOMIASIS RESEARCH ORGANIZATION

Telegraphic Address :
 "TINDELAB" Lohumbe
 In reply please quote

TINDE LABORATORY,
 P.O. LOHUMBO,

No. 1b/46

Feb. 9th.... 1956

Dear Dr. Apte,
Thank you very much for your letter of 4th.
Feb. (SS/11/A/209).

Dec. 18/97 14 Nov. 1897). I am very pleased to hear that you will be probably going to Lake Tanganyika and I shall look forward to coming with you. I do hope you will be sure to. If not, I should be very willing to try and do it for you but I should much rather we could both go.

I am flying up to Tororo on the 17th and shall be back here by the beginning of March.

I should be grateful if you could tell me what equipment I should require (besides a bathing costume). Tents, campbeds, stoves, etc. Both Dr. Willett and I want a strain of T. gambiense so I should bring a few rats. Do you think there would be much chance of getting a

When I return from Toronto I shall contact you as soon as possible.

Yours Sincerely,

Indica Abut.

I am afraid that the trip to the Zambian area, Kagame, is now definitely out as far as I am concerned. The new launch was just a month too late in arriving and although it is now all at Kigoma - in bits - it will take some time to put together.

I have been thinking very carefully over the question of your coming back, but have come to the conclusion that it would really be better if we can leave it until get back from leave and then go together if that time would suit you. I return in early July and would be ready for Kagawa by about the last week in that month, unless something with an even greater priority cropped up while I am away.

This is not because I do not think you could cope with the immense task of it of course, but I feel nothing more than that except the rather boring job of supervising the details of sterility injections, diagnostic procedures and so forth - but in all this field work there is so much outside stuff to arrange - transport and all the rest of it, that it is just not fair to ask you to take it on. There is, too, the question of your working completely fresh with a team of ones quite unknown to you. I now automatically know them and their capabilities and it seems easy to me - but I am afraid that you might find it otherwise however carefully I prepared things. If difficult that drop up you would be almost completely cut off from help. Once the launch which brings us to Karguq goes back to Kirova - which it usually does the same day, there is only chance communication (24 hours to Kirova) with the outside world, unless we arrange to go to the air base. I hope that you will not mind. I shall still look forward to your going together, and after you have once been with me to see the ropes I assure you that I shall be asking you to stand in for me again.

F. I. C. Applied
Cours 500 Series.

Tinde research laboratory is well documented for the outstanding research on trypanosomiasis, some of the documentation being (Ashcroft, 1959; Butt, 1947; Corson, 1931, 1936, 1937, 1938, 1939; Maclean, 1932; Vanderplank, 1941). Also according to the letter shown in Figure 2.11 it is assumed that one of the visits to Kagunga or another gambiense focus was made, and although this existing documentation suggests the presence of Gambian sleeping sickness there is still not enough evidence to affirm Gambian sleeping sickness in Kigoma (Tanzania) between 1924 and 1958. It is unclear why in all these research documentations there is so little information to show studies conducted either in Tabora, Shinyanga or Tinde laboratories using gambiense strains of trypanosomes, and these two research centres in Western province share a common border and also the transport network has always been very good. There was a railway communication between Kigoma and Mwanza through Tabora and Shinyanga constructed during colonial times.

After Independence (1961) most of the control programmes which were in place during colonial era collapsed due to either lack of stable source of funding or shortage of enough qualified staff to manage the programmes or both (Report, 1964; Tsetse Report, 1960). The *Palpalis* group which made a comeback to the gambiense focus are probably still present and in large abundances as there are no sustainable control interventions in place. It is assumed that if *T. b. gambiense* was present in the region, there are chances that it would have also made a come back especially during this time when the control measures did not exist.

2.6 Conclusion

All the evidence discussed in this chapter suggests that there was a possibility of introduction of *T. b. gambiense* sleeping sickness into Tanzania from the shores of Lakes Victoria and Tanganyika, because the disease was introduced from the Belgian Congo (now DRC).

However, the bulk of the disease in Tanzania has always been the Rhodesian sleeping sickness. Tanzania needs to remain vigilant about the possibilities of re-introduction of *T. b. gambiense*. Hence, there is an urgent need to strengthen surveillance activities particularly in the former foci and other risk areas, such as DRC border where vectors are still available.

2.7 Study Limitations

The review observed that storage is a big problem in Tanzania, also the little available data are not consistent with the situation which makes it difficult to track the records and conduct a proper analysis, to confirm when exactly the disease was first recorded in Tanzania and also to affirm existence of Gambian form of sleeping sickness in Tanzania, either in the form of historical patient genetic materials or old patient case notes which would allow answer the question regarding existence of Gambiense sleeping sickness in Tanzania. Therefore based on the diagnostic technique used in Tanzania in the past which were mainly microscopy and the inconsistency and data storage this review was not possible to find enough evidence to confirm either the exact period when sleeping sickness was first recorded in Tanzania or confirm the Gambian sleeping sickness existence in Tanzania from the existing archive.

CHAPTER THREE:

ESTIMATING RHODESIENSE SLEEPING SICKNESS UNDER- REPORTING IN URAMBO DISTRICT TANZANIA

3.1 Introduction

In 2000, all 192 United Nations member states unanimously pledged to meet eight Millennium Development Goals (MDGs) by the year 2015. By definition Millennium Development Goals are eight international development goals that 192 United Nations member states and at least 23 international organizations have agreed to achieve by the year 2015. They include reducing extreme poverty, reducing child mortality rates, fighting disease epidemics such as AIDS, and developing a global partnership for development. However, though the MDGs do not explicitly address the neglected tropical diseases, these neglected tropical diseases share a high prevalence in rural and poor urban regions of low-income countries (Sachs and Hotez, 2006). Among other things addressed in the agenda are the explicit goals of eradicating extreme poverty and hunger (MDG-1) and ensuring environmental sustainability (MDG-7).

Communicable diseases are overarching issues for sustainable development rather than exclusively health matters, as evidenced by the high long-term costs, loss of productivity and social burdens associated with illness and disability from neglected tropical diseases, which go beyond the usual economic analysis of ill health. The goals cannot be fully achieved without an integrated approach, which will target prevention and control of the neglected tropical diseases and some which are zoonoses. In designing these approaches, the expertise of medics as well as vets must be considered as an important aspect in order to achieve substantial outcome in the control. Suggestions have been made, that targeting control interventions towards proper investigation and treatment of livestock which carry zoonotic infections are suitable options in preventing further transmission for most of these disease in both humans and animals (Welburn *et al.*, 2001a)

Surveillance has been highlighted as an important tool for the prevention and control of neglected tropical diseases.

In realizing the importance of this tool, World Health Organization Regional office for Africa in 1998, developed the Integrated Disease Surveillance and Response (IDSR) strategy, as an approach to build nationally-owned sustainable disease surveillance systems among its 46 member states (WHO-AFRO, 1999). The primary goal of IDSR was to strengthen public health surveillance and response to priority infectious diseases at the district level, second was to integrate surveillance with laboratory support, and finally to translate surveillance and laboratory findings into specific and timely public health actions. Indeed IDSR is an important tool, particularly for developing countries where resources are limited, and also emerging and re-emerging infections continue to pose severe threats. Especially since pathogens develop drug resistance (Bailey *et al.*, 2005; Nsubuga *et al.*, 2002). Hence early detection is an important step towards preventing complications, which are likely to arise from improperly managed diseases in developing countries. Unfortunately, despite the serious threat posed by neglected diseases, the majority of the existing national surveillance systems fail to offer neither timely detection nor effective response to many of these diseases (Nsubuga *et al.*, 2002; Sandiford, 1992).

Human African Trypanosomiasis (HAT) or sleeping sickness is one of the severe disabling zoonotic infections, and one of Africa's most prevalent and economically devastating illnesses. It is also one of the most neglected vector-borne diseases, affecting poor populations in remote areas of sub-Saharan Africa. Neglected tropical diseases usually affect the marginalized and impoverished rural populations, and have the tendency of maintaining a very low profile. As a result such diseases are often left out when most of the public health agendas are formulated (Banerji, 2003; Trouiller, 2002). Since the disease affects mainly poor and take a low profile in addressing health agendas, it is most likely to be under-reported, compared to other diseases (Komba *et al.*, 1997; Mbulamberi, 1989b; Odiit *et al.*, 2005; Okia *et al.*, 1994).

Tanzania witnessed decades of devastating suffering from sleeping sickness epidemics which occurred between 1920s – 1960s (Fairbairn, 1948; Moloo *et al.*, 1973).

Sadly, it is still among the most severely affected countries, and also some districts, which recorded substantial number of cases in the past, are among the few districts where the disease is still present. Furthermore, the disease has recently re-emerged in two districts of Mainland Tanzania, where it was initially controlled (Kibona *et al.*, 2002).

In order to strengthen communicable disease surveillance and to allow health teams to respond more quickly to diseases, the Ministry of Health of the United Republic of Tanzania adopted a IDSR strategy, as one of the five approaches used in country's Health Management Information Systems (HMIS) MTUHA in Swahili, the national language. HMIS particularly IDSR has been praised for having good communication and coordination qualities with other sectors in terms of sharing information and resources, however, they been challenged for several inadequacies (Rumisha *et al.*, 2007). First, the systems were found to be unable to receive reports from facilities timely, second they were not able to manage the received reports at the district levels and third, they were unable to monitor their performance of the surveillance systems (Rumisha *et al.*, 2007). Another big concern, which was likely to contribute to the disease under-reporting, is that the system does not provide option to capture all diseases occurring at the facility level. Some of the diseases including most of the neglected diseases which do not feature among the top ten priority diseases of the facility's catchments are, reported under others, meaning that such a disease will definitely not feature in the district records especially in communities where the disease is not among the major concern.

Several suggestions have been given for the current under-estimation of neglected tropical diseases, and they have been categorized into two main groups as follows: Firstly most of these diseases which are also zoonotic are inherently difficult to diagnose due to the fact that they are often not exhaustive and unevenly spread geographically and/or are known by one locality but unknown by another.

They share symptoms with many other common diseases, and they have complex definitive diagnosis, furthermore the reliable, cheap diagnostic tests are currently unavailable, and secondly, the channels through which disease would normally be reported do not function properly and effectively (WHO, 2006a). For many years now, there has been very little investment on research and development of drugs to treat neglected communicable diseases (Trouiller, 2002), that affect mostly the poorest communities, such as sleeping sickness.

The reason for this is mainly due to the fact that there is very little revenue from such investments. Public research institutes in the industrialized world do not view HAT like many other neglected diseases as either a priority or a major threat to their populations, and research-based drug companies do not pursue promising compounds for drugs to treat these illnesses because of an inadequate return on investment (MSF-DND, 2001). It has also been documented that HAT is a disease that affects only isolated rural poor communities and in most cases it is either missed or misdiagnosed on the first health facility visit (Picozzi *et al.*, 2005; Welburn *et al.*, 2006). Besides it relies on low sensitive techniques under field conditions such as microscopy which has been a major concern, as it makes it more difficult to estimate the true occurrence of the disease (Cattand *et al.*, 2001; Picozzi *et al.*, 2005).

The concept of under-reporting (i.e. incomplete coverage) of different infectious diseases has been conducted both in the developed as well as the developing world. However, the accuracy of predicting under-reporting of diseases using assumption and proportions of reported cases from hospital records has recently been challenged due to the unreliability of the data used. In most cases, under-reporting calculations use single value estimates reported at each step which are later multiplied and the inverse taken. This does not give room to understand how randomly the data was collected, the situation which may introduce some degree of bias to the calculations (MacDougall *et al.*, 2007). Over the recent years, many studies on the quantification of disease under-reporting have been conducted both in developed as well as developing countries, using different approaches.

Among the few methods used in different places are the capture-recapture technique which was used to estimate malaria under-reporting in the Netherlands (N.A.H. Van Hest, 2002). In the United Republic of Tanzania (Cleaveland *et al.*, 2002) developed a decision tree model for predicting probability of rabies death following the bite of a suspected rabid dog. Following the achievements of these advancements, these methods were adopted in studies for re-evaluating rabies burden in Africa and Asia (Fevre, 2005; Knobel *et al.*, 2005; Picozzi *et al.*, 2005). In low prevalence areas of Piedmont Region of Italy, Baussano *et al.* (Baussano, 2006) studied under-reporting of tuberculosis, using record linkage of multiple information systems to assess the performance of the surveillance systems. Subsequently they conducted capture-recapture analysis to estimate TB incidence.

In the Netherlands studies using analysis of Pyrazinamide use was used for estimating TB under-reporting (van Loenhout-Rooyackers *et al.*, 2001). Serious under-reporting of visceral leishmaniasis (van der Werf *et al.*, 2003) through passive case reporting has been documented in Bihar India, where Singh and colleagues conducted active house to house surveys to estimate the incidence of VL in endemic areas of India and compared the results to passive surveillance cases reported in public health facilities (Singh, 2006). In Britain, a study on malaria under-reporting was achieved using a review of all telephone enquiries from doctors seeking advice from their colleagues at the hospital for tropical diseases (HTD), London (Davidson, 1993).

In Uganda, Odiit *et al.* (2005) developed a decision tree model for sleeping sickness under-reporting. Using this model, 39% of HAT cases were under-reported with approximately 92% unreported deaths due to HAT occurring in rural communities of Uganda (Odiit *et al.*, 2005). The measure of early to late stage presentation presented in this model was found to be useful, hence it was recommended for the use in other rhodesiense sleeping sickness endemic areas across sub-Saharan Africa.

However, it was advised to take pre-cautionary measures in drawing conclusion with the results of the model, as the data used in its development was obtained from an area with a relatively low probability of under-reporting because of a better infrastructure and a better health services when compared to other sleeping sickness areas of sub-Saharan Africa .

Tanzania National Health Policy is based on the concept of Primary Health Care (PHC). Its overall objective is to improve the health and well being of all Tanzanians, with the main focus on the most risk, and to encourage the health system to be more responsive to the needs of the people (Ministry of Health, 1994). However, it has been difficult to achieve the expected goal, particularly in rural settings where insufficient resources both human (in term of staff) and materials (equipments, drugs and finance) have always been problematic. Furthermore some communities have been ignored by the health authorities, either unwittingly or perhaps due to lack of adequate resources and/or lack of sufficient awareness or sometimes even both. Most of rural health facilities have no capacity to diagnose most infectious diseases including HAT. Recent studies suggest that even in areas with a reasonable number of staff, not all of them can properly diagnose and treat cases of sleeping sickness (Adams *et al.*, 2006). This situation exposes rural communities to risk of disease under reporting, and as a result this impinges on the rights of the people with less income to obtain basic health services, such as early detection of diseases which are treatable, including sleeping sickness. As a result, these diseases are severely underreported and consequently they receive less prioritization. This therefore exposes HAT to the high risk of been under-reported.

World Health Organization in its 1997 assembly passed a resolution to eliminate HAT in all endemic countries by 2015 (WHO, 1997). Although this may look very ambitious given the existing resources (WHO/AFRO, 2005), it is an achievable goal particularly if all required logistics are timely put in place.

The meaning is that in order to achieve the targeted goal, there is an urgent need to look for the best ways of preparing multi-sectorial integrated approaches, which will allow proper utilization of the little available resources, and these will require full community awareness and commitment. Besides there have been significant achievements in the control of HAT in the past twelve years. Worldwide cases reported for the past five years show a remarkable reduction in the total number of new cases reported per year, which reached 17,500, and a new estimated cumulative rate of 50 000 – 70 000 cases (WHO, 2006b)

In Tanzania, a significant reduction in total number of cases reported each year from 422 in 1995 to 157 cases in 2004. However, it's unlikely these figures represent the true disease situation in the country considering the factors associated with under-reporting which comprises the bulkiness of this chapter. It have been observed over the last few years, that HAT cases are not regularly reported to the coordinating centre, Tabora as they should have been and there is no documented evidence which changed this mandate. The system of notification discussed in detail in Chapter II required all treatment centres to report every case of sleeping sickness diagnosed in their health facilities to the National Institute for Medical Research, Tabora. This makes it difficult to track back records of all sleeping sickness cases in the country, hence providing room for possible under-reporting. The 157 cases reported here were based on passive surveillance data reported from only three regions of western Tanzania Kigoma, Tabora and Rukwa with over 95% reported from the districts of Mpanda (Rukwa) and Urambo (Tabora Regional Profile). Furthermore all these cases were diagnosed and treated in one health facility the rest of the health facilities reported no cases of HAT to the district hospitals.

The present study is concerned about the level of rhodesiense sleeping sickness under-reporting. Like many other countries of sub-Saharan Africa, Tanzania which had brought the disease close to elimination in 1960s (using control measures discussed in Chapter I), is facing a dramatic resurgence, even in areas where it was initially well controlled (Kibona *et al.*, 2002).

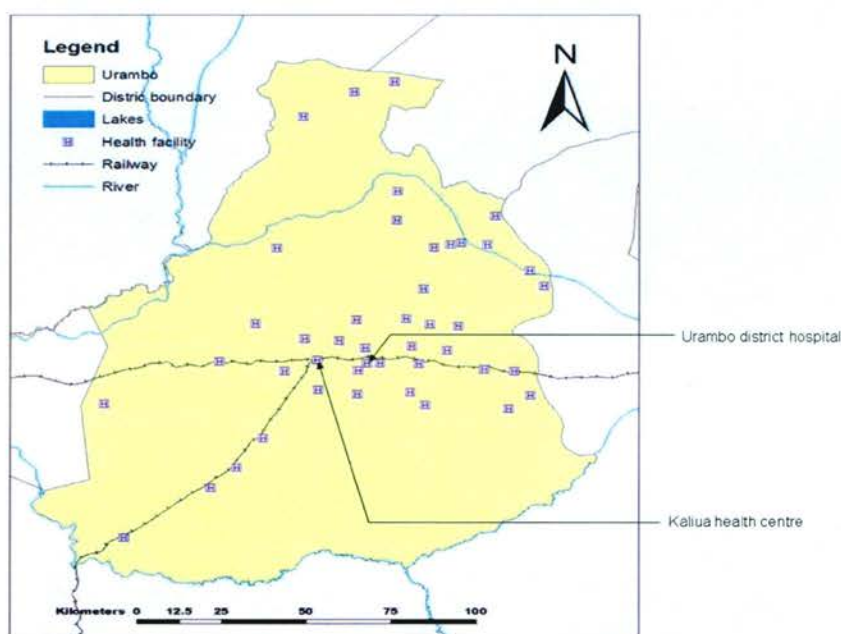
It therefore becomes more difficult to obtain the accurate occurrence of the disease from the local levels. Also there is no evidence of sufficient research conducted to assess the needs of respective communities; this may result in inadequate and inappropriate resource allocation, as well as failing to target the diseases in question. Moreover, the majority of the recent relief programs clearly emphasize implementation of primary health care (PHC) to focus on prevention programs such as immunization. This again does not capture most of the neglected diseases such as sleeping sickness, highlighting the urgent need to estimate the level of neglected diseases under-reporting. The findings of which will provide useful inputs to be incorporated in the quantification of disease burden imposed on local poor communities.

3.1 Material and Methods

3.1.1 Study Area and Population

The study was carried out in Urambo district in Tabora region, western Tanzania. The District occupies an area of 25,995 square kilometres and is located at latitude ($4^{\circ} 00''$ - $5^{\circ} 53''$) S and longitude ($30^{\circ} 00'$ - $32^{\circ} 37''$) E. The district is divided into four Administrative divisions, which are Urambo, Ulyankulu, Usoke and Kaliua; twenty six wards and one hundred and four villages. According to national census the total population for the district is 369,329 and 63,256 households (National Bureau of Statistics, 2002).

Figure 3.1 Map of Urambo district showing the location of all health facilities



3.1.2 Health Profile and Sleeping Sickness in Urambo District

Urambo is served by one district hospital, four health centres and thirty five dispensaries. The health facilities are distributed as follows: Urambo division one hospital and nine dispensaries, Ulyankulu one health centre and ten dispensaries, Usoke two health centres and two dispensaries, Kaliua division one health centre and fourteen dispensaries. Three out of the fourteen dispensaries of Kaliua have not been functional since construction was completed more than three years ago due to lack of staff. In the district, drugs to treat HAT are only supplied to Kaliua health centre, therefore all sleeping sickness patient are referred to Kaliua for treatment. The decision to supply drugs only to special centres was reached due to several factors; first Kaliua is located close to all sleeping sickness endemic villages in the district, second the centre has the capacity to diagnose, confirm and treat cases of sleeping sickness and third the centre has enough space to admit and manage all cases of sleeping sickness.

Beside the factors listed above, the decision was reached as part of an attempt to ensure proper drug utilization and monitoring following severe drug shortages, which hit the country in late 1990s. Urambo district has not experienced sleeping sickness since 1996.

3.1.3 Data Collection Methods

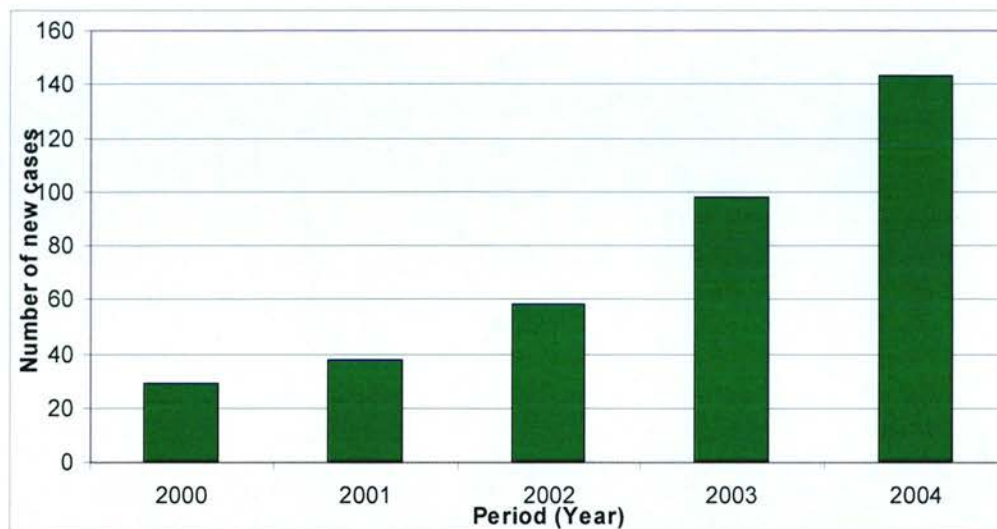
The National Institute for Medical Research, Tabora research centre is mandated at coordinating and documentation of all sleeping sickness activities in the United Republic of Tanzania. However, over the last few years a significant number of cases of sleeping sickness are not regularly reported to the centre from all treatment centres as used to be. This therefore makes it difficult to track back and achieve proper records of all sleeping sickness cases in the country. Apparently there is no written documentation which amended the card notification. The data used in the current study are therefore based on active and passive surveillance data, extracted from Kaliua health centre in-patient registers.

This data also includes all patients diagnosed during active surveillance exercises, as cases are always referred to HAT treatment centres such as Kaliua HC for treatment. In order to be able to estimate the level of rhodesiense sleeping sickness under-reporting in Tanzania, the detailed retrospective study of sleeping sickness cases diagnosed and treated at Kaliua health centre between January 2000 and December 2004 was conducted.

3.1.4 Case Definition

A case of HAT for this study was defined as “a person presented for treatment at Kaliua health centre between January 2000 and December 2004, with clinical and parasitological confirmation of sleeping sickness using WHO criteria for diagnosis of sleeping sickness (National Bureau of Statistics, 2002), or having white cell count $>5\text{mm}^3$ for late stage).

Figure 3.2 Total number of new sleeping sickness diagnosed and treated in Urambo district



Between 2000 and 2004, 328 cases of sleeping sickness were diagnosed at Kaliua health centre (Figure 3.1) above, out of them 69 reported in early stage of the disease, 237 in late stage and 22 patients were not staged. Out of them 15 patients died.

In cases where patients had more than one hospitalization for the same condition all duplicates were removed based on first occurrence per patient. This was simply achieved using patient medical record numbers. All this information was fitted in the decision tree model structure for sleeping sickness under detection (Odiit *et al.*, 2005).

3.1.5 Model Structure

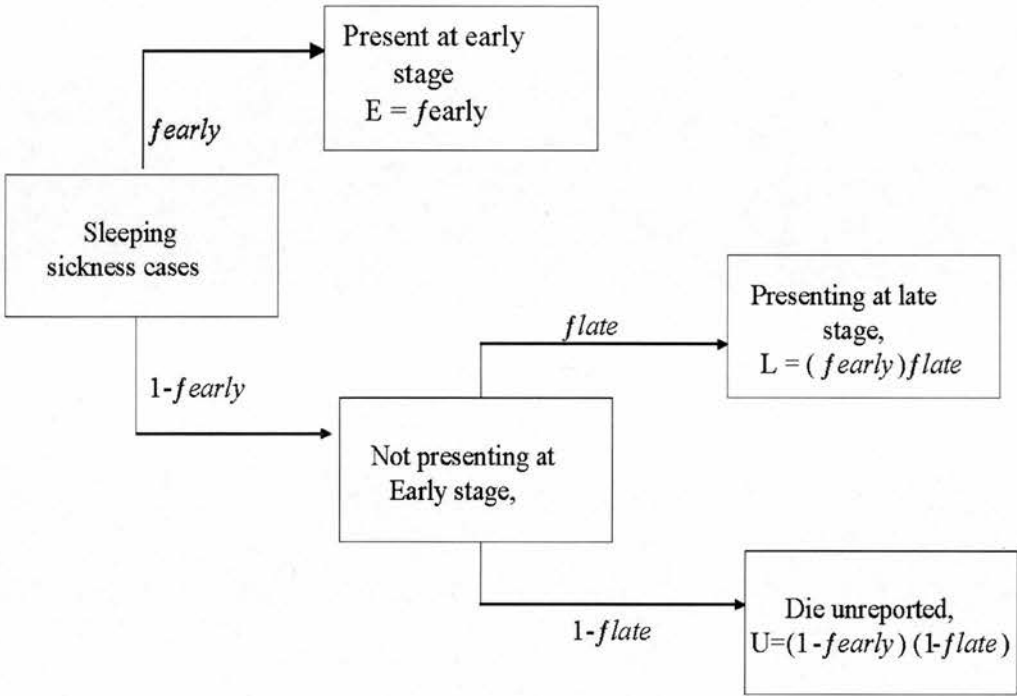
According to (Odiit *et al.*, 2005), the decision tree model structure shown in Figure 3.3, and its parameters shown in Table 3.1, works using conservative assumption that there is no increased mortality due to early stage sleeping sickness, in terms of estimating the proportion of sleeping sickness that die undetected.

The model takes into account that clinical presentation of sleeping sickness progresses from early to late stage and subsequent death especially if no treatment is provided. It also assumes that there are little chances of increased possibility of death in the early stage when compared to late stage. The model structure comprises a series of probabilities and it underwent two main structural stages: under-detection model structure and structure for estimating undetected deaths.

3.2 Structure for Under-Detection Stage

This was achieved using survival analysis using the Monte Carlo Simulation. The list of all possible probability outcomes are as follows: A proportion of sleeping sickness cases that did present at health facility, will present as early stage patients E , with a probability f_{early} . The other proportion of cases that do not present at early stage (\bar{E}), will either present as late stage cases (L), with a probability f_{late} , or die undetected (U), with a probability $1-f_{late}$. Therefore, the model has only three possible outcomes for each sleeping sickness case: (1) presentation with early stage disease, E , with probability f_{early} , (2) presentation with late stage disease, L , with probability $(1-f_{early})f_{late}$ or (3) dying undetected, U , with probability $(1-f_{early})(1-f_{late})$, where E , L and U are all proportions and sum to 1 (Odiit *et al.*, 2005).

Figure 3.3 Structure of the decision tree model for rhodesiense sleeping sickness.



The boxes are the different outcomes of sleeping sickness cases. The arrows show the directions of clinical progression. Probabilities for each stage of the model are shown in italics.

The coefficient for under-reporting; U.

Under-reporting was quantified by the under-reporting coefficient (U), which is calculated using the formula:

$$U = (1-f_{early}) (1-f_{late})$$

Where, *f_{early}* is the ratio of early cases observed and the sum of detected and undetected cases.

And *f_{late}* is the probability of sleeping sickness cases presenting at late stage.

Figure 3.4 Summary of definition of decision tree model parameters

Model state	
E	Proportion of sleeping sickness cases presenting as early
\bar{E}	Proportion of sleeping sickness cases not presenting as early
L	Proportion of sleeping sickness cases presenting as late, not early
E/L	Ratio of early to late cases – estimated from empirical data
Rates	
l_t	Hazard function for onset of symptoms at which late stage cases present at health facilities – estimated by survival analysis, using a Weibull distribution with parameters αl and λl
u_t	Hazard function for onset of symptoms at which late stage cases die – estimated by survival analysis, using an exponential distribution with parameter λu
Probabilities	
f_{early}	Probability of presenting at early stage, calculated using E/L and f_{late}
f_{late}	Probability of presenting at late stage, calculated by numerical simulation of integrals of the rates at which late stage cases present at health facilities, l , and die of sleeping sickness, u
Outputs	
U	Proportion of sleeping sickness cases that die undetected
D	Number of undetected deaths (cases)

3.3 Results

3.3.1 Model Prediction

A total of 366 (69 early, 275 late and 22 unstaged) sleeping sickness cases were diagnosed and treated at Kaliua health centre in Urambo district between 2000 and 2004. The observed ratio of early to late stage sleeping sickness cases was 0.25. The decision tree model for under-reporting predicted that apart from the 366 reported cases, the probabilities of reported and unreported late stage deaths were 56% and 44% respectively. The model also predicted that 233 cases were unreported deaths, making a combined total of reported and unreported cases to 599. The ratio number of unreported deaths per recorded deaths in Urambo during this period was 16 (Table 3.2).

3.3.2 Outputs of the Decision Tree Model for Under-Detection

The outputs of the model show a slight increase from what it predicted, although all the output results lie within the range of the confidence intervals to what was predicted. These findings suggest that on average a proportion of 11% (95% CI: 09, 13) of all HAT cases presented at early stage, while 43 % (95% CIs: 38, 51) presented at late stage. In general 45% (95% CI 36, 53) of all sleeping sickness were undetected death (Table 3.3). This is an average of 299 cases (95% CI: 194, 389) which died unreported in the district. The model also suggested that an average proportion of reported to unreported is 18 (95% CI: 13, 25), in other words this is to say, for every reported sleeping sickness case an approximately 18 others went unreported in Urambo district. The results therefore suggested that apart from the 15 cases which were reported deaths, 299 (95% CI: 194, 389) more cases went undetected and died somewhere within the community making a total number of deaths in Urambo district to be 314 (95% CI: 209, 404). Hence the new number of reported and unreported sleeping sickness cases totals 643 (95% CI: 538, 733).

The interpretation of the model outputs is made bearing in mind, that the data used to develop the model was obtained from a health facility in south east Uganda according to Odiit (2005), health facility form which data was collected had a better condition (well equipped with resources) as compared to other disease endemic areas of sub Saharan African such as most of facilities in Urambo district. The use of this model in this chapter is to provide an overview of the possible HAT situation in Tanzania. It has been used in this chapter with great caution with the assumption that the disease situation across eastern Africa follows the same patterns as in Uganda.

Table 3.1 Decision tree model inputs and predicted outputs

Observed	Variable	
Number of early stage patients	E	69
Number of late stage patients	L	275
Number patients not staged	N	22
Ratio E/L	E/L	0.25
Total presenting	P	366
Total deaths	M	15
Model predictions		
Probability of a late stage case presenting	S*	0.56
Probability of a late stage case dying before presenting	U*	0.44
Outputs		
Probability of case presenting early	f	0.12
Probability of case presenting late	(1-f)S*	0.48
Probability of case dying undetected	(1-f)U*	0.38
Ratio E/L	f/(1-f)S*	0.25
Probability of reporting	f+(1-f)S*	0.61
Total cases	T	599
Total undetected sleeping sickness deaths	D	233
Number of unreported deaths per recorded death	D/M	16

Table 3.2 **Summary of actual decision tree model outputs**

	Model output		
	Mean	95% CIs	
Proportion presenting at early stage $E = f_{early} = 69 / (344 + D)$	0.11	0.09	0.13
Proportion late stage presentation $L = (1 - f_{early})f_{late} = 275 / (344 + D)$	0.43	0.38	0.51
Proportion of undetected deaths, $U = (1 - f_{early})(1 - f_{late}) = D / (344 + D)$	0.45	0.36	0.53
Proportion of undetected to detected deaths, D / M	18.00	13.00	25.00
Ratio of early to late stage, E / L	0.25	0.23	0.26
Total number of undetected deaths, D	299.00	194.00	389.00
Total number of detected and undetected deaths, $D + M$	314.00	209.00	404.00
Total cases	643.00	538.00	733.00

KEY: CIs = Confidence intervals

Note: All unreported sleeping sickness cases are assumed to be unreported deaths

The model also suggests that 25% (95% CI 23, 26) is the average of early to late stage ratio. Using these ratios as well as 45% (95% CI 36, 53) which is the proportion of undetected deaths, the estimation of the number of sleeping sickness deaths which would have occurred in Tanzania as well as other *rhodesiense* sleeping sickness in sub Saharan Africa was achieved as follows:

Between the same period of 2000 and 2004, a total of 1099 and 3168 *rhodesiense* sleeping sickness cases were reported from Tanzania and worldwide respectively (WHO, 2006b). If it is assumed that these HAT cases follow the same patterns of disease as Urambo, which is 0.25 (95% CI: 23, 26) early to late ratio, and 45% under-reporting, then it means that 495 and 1425 HAT cases would have died in Tanzania and worldwide (sub Saharan African) respectively due to *rhodesiense* sleeping sickness under-reporting during the same period.

3.4 Discussion

Findings from the current study suggested that levels of rhodesiense sleeping sickness under-reporting in Urambo (Tanzania) are very high, a little bit higher than what was observed in Uganda's study (Odiit *et al.*, 2005). These higher levels are likely to be the results of infrastructure in Tanzania in comparison to Uganda (Odiit *et al.*, 2005), where data to develop the model was obtained. This does not necessarily reflect the actual situation in other rhodesiense sleeping sickness endemic areas of sub Saharan Africa.

The model works by assumptions and, it is assumed that, the 15 patients who died in Urambo were admitted at a very late and serious state and died before they received any kind of treatment. However, in a normal situation this is very unlikely. There are many misdiagnoses as well as delayed diagnoses in most of the rural health settings, but it seems unlikely that all 15 patients received no treatment. It is possible some of them may have received treatment but still died due to a number of factors such as drug sensitivity, severe anaemia or other concomitant conditions. Also from the original data it was observed that 6.0% (22 out of the 366) of cases, were not staged which makes it unclear whether these un-staged patients did receive any kind of treatment. The treatment of HAT entirely relies on proper stage determination. Suramin is normally used for early stage and melasorprol for late stage for rhodesiense sleeping sickness. The possible assumption in such a situation is that patients were diagnosed at Kaliua health centre, but received treatment elsewhere or they received no treatment for some unclear reasons and died in the rural areas. Presently there is no evidence of any traditional treatment for sleeping sickness in Tanzania so any untreated case would have died.

The model suggests that an average of 299 (95% CI: 194, 389) were undetected deaths in Urambo district, for the period between 2000 and 2004. Several factors are likely to be associated with such high rate of under-reporting.

These include lack of enough health facilities with the capacity to diagnose and treat the disease, staff shortage, long distance travelled by the sick people in search for health facilities which can manage the disease and inadequate awareness among endemic communities. It is also very possible that, some of the unreported deaths may have attended some of the health facilities during this period, probably with clinical presentation resembling sleeping sickness but were misdiagnosed to several other vector borne diseases presenting in a similar way. As a result they were allowed to go home without receiving proper investigation and ultimately treatment, this allowed the disease to develop further resulting in death. It is suspected that majority of the undetected sleeping sickness die in the rural communities due to unavailability of facilities to diagnose and treat the disease.

Knowledge of the disease is also an important factor which may have contributed to high level of disease under-reporting. Some cases present in a very obvious way, which can give a direct clue, assuming one has a basic knowledge of the disease. In some areas, particularly where the current study was conducted, most of the health facilities were severely understaffed, while some are manned by nurse auxiliaries who have very limited clinical knowledge. Also some facilities are not staffed at all (NIMR, 2004). Out of the fourteen dispensaries visited in the study area were not staffed or lacked equipment (not opened yet), this situation may have existed since they were constructed more than three years back. All the three dispensaries are located in sleeping sickness endemic villages. This may probably be one of the reasons for the high levels of disease under-reporting in the district. It is appreciated that the willingness to contribute towards controlling diseases among communities exist; the only problem is that authorities had a different priority when communities planned to build the health facilities, as it seems unlikely that district health authority was consulted during the planning of the unstaffed facilities. This therefore stresses the need for community involvement in health priority setting in the rural areas (Makundi *et al.*, 2005).

A number of logical research questions have arisen following the findings of this under-reporting study. It is therefore important to start considering possibilities of conducting under-reporting studies in livestock disease endemic areas, especially if the intention is focused towards increasing the degree of understanding of epidemiological dynamics for African trypanosomiasis. This will increase the capacity for early detection and treatment of neglected zoonoses, hence proper planning and strategise the management and control of these diseases. It has been documented that proper control measures against human sleeping sickness should be directed towards animal reservoirs through chemotherapy (Welburn *et al.*, 2001a).

Outbreaks of sleeping sickness have been documented in various parts of Africa (Moore and Richer, 2001; Moore *et al.*, 1999; Smith, 1998; Van Nieuwenhove *et al.*, 2001) and from the estimates of the level of under-reporting; it is obvious that many patients died in the past and will continue to die as a result of sleeping sickness under-reporting in the rural areas of disease endemic countries. Studies conducted in Zaire, observed the same order of magnitude in mortality caused by AIDS and HAT (Ekwanzala *et al.*, 1996) and also the number of HAT related deaths which occurred in 1994 was at least 80 times higher than the total number of deaths recorded during the 1995 Ebola fever epidemic in Kikwit (CDC, 1995). Moreover HAT management is conducted in a controlled way due to the toxicity of the drugs used. In Tanzania the drugs are only available in the treatment centres (drugs are neither available in the drug stores nor private clinics) and the assumption is, no treatments are conducted outside hospital settings or treatment centres. This excludes any possibilities of self-medication, meaning that all sleeping sickness patients who did not attend treatments centres died, as sleeping sickness is fatal if left untreated.

In connection with the current findings, several other factors can be suggested in association with high levels of rhodesiense HAT under-detection in Tanzania.

First; the majority of communities under study cannot afford to pay transport to reach the health facilities with capacity to diagnose and treat sleeping sickness. Most of endemic villages in Urambo are remotely located. The road communication between these villages is very poor and as a result the majority are not accessible throughout the year. The only reliable means of transport connecting HAT endemic villages and the treatment centres is the train, which is again not always reliable. In most cases there are serious delays and sometimes trips are even cancelled without providing prior notice to travellers. The situation therefore poses very serious challenges to these communities, which sometimes forces them to carry their patient on a bicycle and travel very long distance through heavy forest, which is also densely infested with tsetse flies.

CHAPTER 4:
QUANTIFYING THE BURDEN OF DISEASE DUE
TO RHODESIENSE SLEEPING SICKNESS IN
URAMBO, TANZANIA

4.1 Introduction

Infectious diseases place a considerable burden on communities and health authorities in developing countries. The highest disease burdens, about 21.4% of global total were estimated for sub-Saharan Africa (World Bank, 2004). The burden of deaths and disability caused by neglected infectious diseases in developing countries also stands very high. In sub-Saharan Africa alone, it is estimated that mortality accounts for 80% of total disease burden. In 1990, it was estimated that out of almost 90% of the global disease burden carried by these countries, only 10% of global health care funding was allocated to them (Murray and Lopez, 1997a). About 15 million (>25%) of the 57 million annual deaths worldwide are estimated to be directly related to infectious diseases (Morens *et al.*, 2004).

Despite remarkable advances in antimicrobial therapies, infectious diseases have claimed millions of lives as well as causing enormous pain, suffering, and disability, in addition they have also created a constant sense of fear and panic in societies (Kombe and Darrow, 2001). Several factors have been identified to be associated with Africa's high disease burden. These are a lack of new tools for timely diagnosis, the long duration of treatment schedules for most of the infectious zoonotic diseases, particularly human African trypanosomiasis (Moore, 2005), physical ecology which favours habitats of most vectors, poor nutritional status resulting from low agricultural productivity and excessive poverty which leads to lack of good quality medical access and finally inadequate disease knowledge which leads to the low awareness of disease situations, particularly in rural areas where high impact of disease burden is often observed.

The emergence and re-emergence of infectious disease has been one of the biggest challenges to scientists in developing strategies for sustainable control measures. Close collaboration, comprising medical as well as veterinary experts is crucial in designing strategies for the control of these diseases, bearing in mind the current existence of wide range of zoonotic infectious diseases (Morse, 1995).

Available evidence suggests that around 61% of the 1,415 species of human pathogenic organisms and 60.3% emerging infectious diseases (Hendrickx *et al.*, 2001) are zoonotic (Cleaveland *et al.*, 2000; Cleaveland *et al.*, 2002; Jones *et al.*, 2008).

Moreover the majority of the emerging infectious diseases 71.8% originate from wildlife (Jones *et al.*, 2008). The biggest number of these zoonotic infections as well as other infectious diseases exist in Africa, particularly in sub-Saharan Africa; this justifies the reason leading to prioritization of Africa for future investment (WHO, 2002a). Human African trypanosomiasis or sleeping sickness which is amongst the most neglected diseases, and one of the prominent zoonotic diseases has also reemerged recently. The current resurgence has been reported in several countries of sub Saharan Africa the most recent ones being Uganda (Ochan, 2004; Smith, 1998), in Tambura county in Sudan (Moore and Richer, 2001), in Tanzania (Kaare *et al.*, 2007; Kibona 2001), and in the Democratic Republic of Congo (Van Nieuwenhove *et al.*, 2001).

About two decades ago there were no reliable epidemiological data-set to support proper identification of priorities for health services and research. However, many countries still maintained reliable information on the traditional vital registration systems to provide data on the number of deaths by cause and the sex, and age of the victims. The Global Burden of Disease project (GBD), a worldwide collaboration of over 100 researchers, sponsored by WHO and the World Bank published its findings in 1993. The widely publicized GBD which is probably a better option presented a bold, new analysis, providing the first quantitative description of the world's health. This study used a new metric tool – disability –adjusted-life-years (DALYs) – to quantify the burden of diseases, injuries and risk factors with a single currency based on years of life lost due to premature mortality (YLL) and years lived in less than full health (YLD) (Lopez, 2001).

DALYs were developed as the unit measurement to quantify the burden imposed by disease and injury on human population for the GBD study (Murray, 1994). It is a generic health gap measure, which combines information about both morbidity and mortality in numbers of healthy years lost. It is a standardized objective normally used in public health as an important measure for different disease conditions.

The morbidity component accounts for the degree and time of morbidity suffered by patients with a particular health condition, whereas the mortality component accounts for loss of life years at different ages due to a particular health condition in a population.

In the DALY approach, a panel of experts assigned a disability weighting to each state of health on a scale from zero which stands for perfect health to one which stands for death (Murray and Lopez, 1996a). In order to be able to calculate burden of a certain disease in a population, the disability weighting is multiplied by the number of years lived in that health state added to the number of years lost due to that disease. The result of this, makes years of life in childhood and old age count less in burden estimations, a discount rate of 3% per year and value of life time is weighted.

The public health burden imposed by HAT was estimated to be 1.5 million DALYs in 2002 (WHO, 2004). The disease is placed 2nd and 4th amongst the most important vector-borne diseases in Africa in terms of mortality and DALYs respectively. The global figure for the burden for sleeping sickness, calculated using a conservative estimate of 50,000 cases per year, is 1.78 million DALYs per year (Murray, 1994). Although small in comparison with the DALYs for the two leading infectious diseases tuberculosis (38.4 million DALYs) and malaria (31.7 DALYs), this is significantly greater than for other vector-borne disease such as onchocerciasis (0.88 million (WHO, 2002b) DALYs) and dengue fever (0.75 million DALYs), and is comparable with the burden due to leishmaniasis (2.06 million DALYs), despite there being some 350 million people at risk to leishmaniasis in 88 countries. The most recent global figures estimate that there were 2.0 million DALYs lost due to HAT (WHO, 2002b). And also it was estimated that HAT is responsible for 48,000 deaths (WHO, 2004). In addition, the HAT figure is largely based on the *T. b. gambiense* form of the disease. *T. b. rhodesiense* is more acute and may therefore impose a greater morbidity than *T. b. gambiense*; this has been observed in similar studies conducted in Uganda and DRC. Findings of these studies, discourage the use of global figures in priority setting at the local level (Kapiriri and Norheim, 2002; Kapiriri *et al.*, 2003; Lutumba *et al.*, 2007)

The burden imposed to communities by HAT has been estimated; the findings from these studies which were conducted at different administrative levels suggested that such estimates are very important for proper resource allocation. A study conducted at the village level in Buma DRC suggested that, without intervention gambiense HAT was responsible for 2,145 DALYs. The intervention carried out by the control programme averted 1,408 DALYs at the cost of US\$ 17 per DALY averted (Lutumba *et al.*, 2007).

In Uganda a study conducted at the district level in Soroti shows that, DALYs lost due to HAT in the district between 1999 and 2005 were estimated at 1405 and 1136 with and without age weighting respectively (Fevre *et al.*, 2008). When 69% under-reporting was incorporated the mean annual DALY burden were 1157 and 86 with and without age weighting (Fevre *et al.*, 2008).

4.1.1 Burden of Neglected Tropical Diseases in the HIV Era

It is known that Acquired Immune Deficiency Syndrome (AIDS) has already significantly increased mortality in many countries, particularly in sub Saharan Africa, and the impact of AIDS upon mortality has grown substantially over the past two decades. Understanding the significance of AIDS in the burden of disease estimation is important particularly in the countries of sub Saharan Africa where more severe AIDS epidemics have occurred. AIDS contributes significantly in reducing the life expectancy of communities living in most of the severely affected countries. The World Bank estimates that because of the AIDS epidemic, life expectancy by 2010 will revert to 47 years instead of the projected 56 years in the absence of AIDS. Besides, communities living in severely affected areas suffer a number of several neglected disease. Hence studying the association between the burden of neglected tropical infections and eventually the impact of HIV/AIDS on these diseases to affected communities is essential for daily planning and monitoring trends locally, nationally as well as internationally. Recent research findings observed that diseases that were once rare such as *Cryptococcus* are now increasing, and HIV-associated diseases are the main cause of bed occupancy in hospitals and deaths in many African countries, with most morbidity and mortality caused by preventable tropical infectious diseases (Corbett *et al.*, 2002).

A large number of clinical observations have indicated that the presence of concurrent infections-sometimes preceding, and often following the HIV infection, and concomitantly, HIV infection may alter the course and manifestations of other infections (Bentwich *et al.*, 2000). However, research conducted so far suggests that there is no direct increased risk of *gambiense* sleeping sickness among HIV infected patients (Louis *et al.*, 1991; Pepin *et al.*, 1992).

There is significant geographical overlap between HIV, sleeping sickness as well as many other neglected infectious diseases in HAT endemic countries in SSA, meaning that even a very small interaction could lead to a substantial impact to affected communities. Available documentation suggests that a combination of HIV and Tuberculosis or HIV and any other neglected tropical diseases impose a double burden to communities particularly in low income countries (Hotez *et al.*, 2006; Msamanga and Fawzi, 1997). However, in most cases the burden imposed by a less common disease tends to be ignored or overlooked. There exist large uncertainties about the course of mortality between high and low income countries particularly sub-Saharan Africa ranging from high income 1% to low income 15-20%. Available evidence shows that sub Saharan Africa is severely burdened by the HIV epidemic, and in connection with this, the impact and the burden imposed to rural household is very significant (Kwaramba, 1998). Moreover the disease tends to affect the household workforce during their best economic productive years, when they are responsible for the highly needed support and expected to provide care to others (Quinn, 1996). HIV infection significantly increases the level of poverty, and as a consequence contributes to increasing the burden of other concomitant diseases to most of the affected communities. Furthermore AIDS deaths are always preceded by a prolonged period of illness and suffering, which gives majority of the sick person sufficient time to utilize available resources on medical care and to move to a preferred place of dying (Urassa *et al.*, 2001). Despite the fact that sub Saharan African countries contain only 10% of world's population, it was estimated that by June 1994, there were 14 million people living with HIV infection (WHO, 1994). AIDS causes a very high burden in terms of DALYs, which were estimated at 14.7 million (World Bank, 1993).

In many developing countries, a significant proportion of deaths may occur in communities without any medical attention, sometimes deaths may be registered without even a medical opinion about the possible cause of death (Mathers *et al.*, 2005). There is also enough evidence that there is a very strong negative association between adult HIV prevalence and life expectancy (McGuire *et al.*, 2005), meaning that HIV infection significantly decreases life expectancy especially in resource poor countries. Neglected tropical diseases account for 57 million disability adjusted life years lost annually in sub Saharan Africa alone, and it is estimated that more than 500 million people are infected by HIV. The burden imposed by these diseases crosses over and affects childhood education as well as economic development, as a result they promote poverty (Hotez *et al.*, 2006). In both developing and developed countries, legal, societal or other reasons may lead to the under-reporting of causes of a sensitive nature, such as suicide or HIV/AIDS (King, 1989; Klatt and Noguchi, 1988). Furthermore, the selection of a single underlying cause of death is frequently problematic particularly in elderly people, who often present with several chronic illnesses that concurrently lead to death.

Treatment of HAT is determined by the type and stage of the disease. Unlike many other infectious diseases which are easily treatable; sleeping sickness is 100% fatal if left untreated. Besides, the only few drugs which are currently available for treating the disease are expensive, contain arsenic and anti-freeze compounds, and were developed more than 70 years ago. Most of the drugs are administered parenterally, some of them are extremely painful when injected, require hospitalization during administration and often ends up with very severe adverse effects (WHO, 1998). Furthermore the patients who do survive the side-effects of treatment, there is still no guarantee of complete cure, as the drug fails in 25-30% of cases in some areas (Hutin *et al.*, 2004).

The United Republic of Tanzania has the misfortune to have not only a number of several active foci for *rhodesiense* sleeping sickness but also a number of other neglected tropical diseases and zoonoses. In addition, both forms of sleeping sickness are believed to have existed in country on different occasions, the last case of *gambiense* sleeping sickness being documented in 1958 (Fairbairn, 1948; Ormerod, 1961).

Over the recent years, the burden of the disease in the country has been compounded by a number of issues including an increased influx of refugees and unstable weather, which forces farmers and big livestock keepers to migrate from place to place in search of suitable environments for agriculture as well as favorable feeds for their herds. Indeed sleeping sickness is a disease of major socio-economic and public health concerns to the majority of rural communities, with over four million people at risk. Endemicity has been reported in 10 regions of mainland Tanzania and between 1996 and 2006 more than 2748 cases were reported, with over 95% of these figures, recorded from only three regions of the western part of the country. In light of these facts, there is an urgent and obvious need to prioritize the little available resources in health interventions by employing the objective measure of the burden of neglected disease.

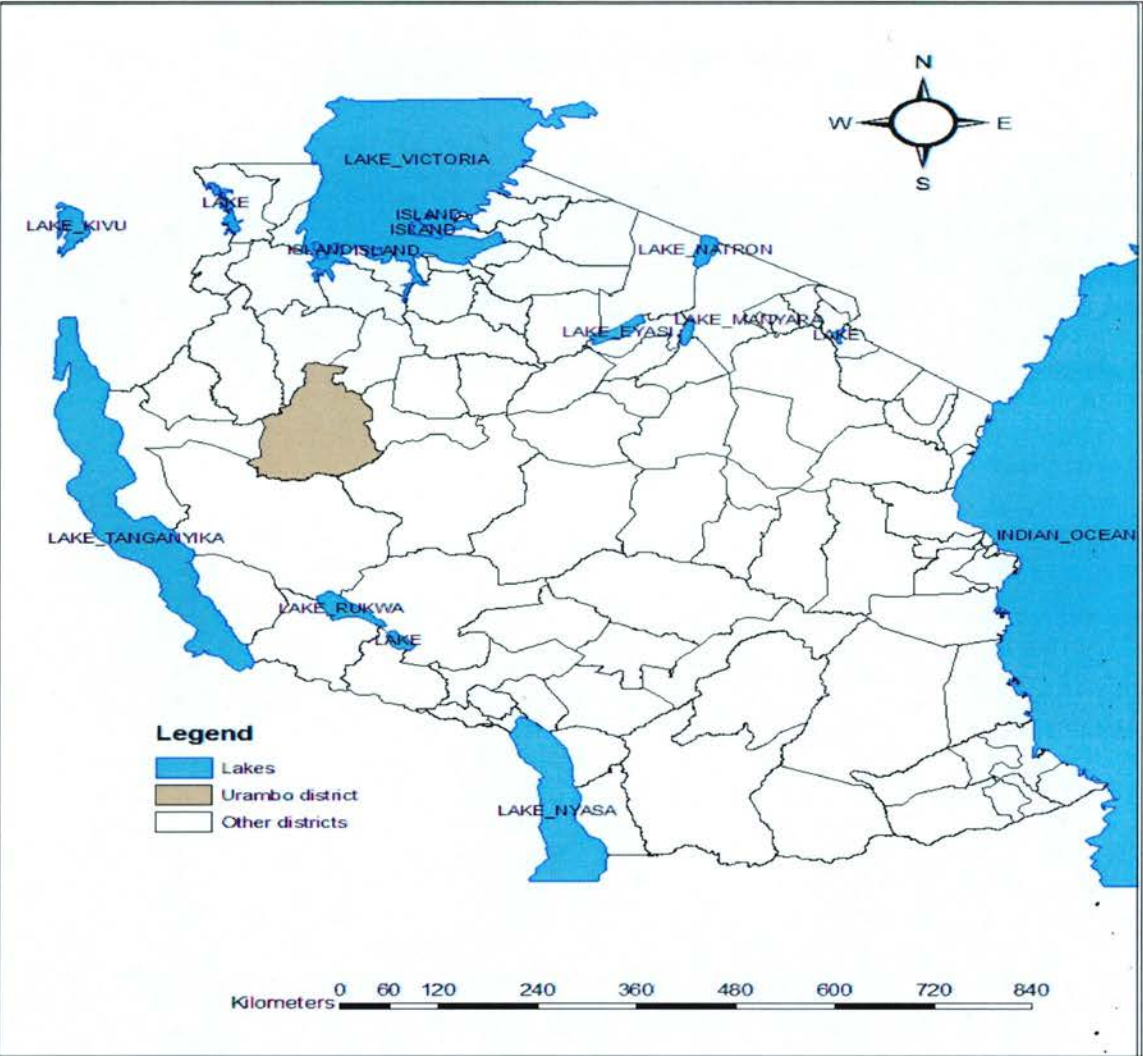
Hence, an accurate estimate of the burden of HAT for Tanzania is urgently required, so as to fill the existing gaps and provide updated information to relevant authorities there by contributing towards the design of sustainable cost-effective control interventions.

4.2. Material and Methods

4.2.1 Study area and population

The study area was Urambo District, Tabora, Tanzania (Figure 4.1). The district is situated in the western part of the country between latitude $4^{\circ} 00''$ - $5^{\circ} 53''$ S and longitude $30^{\circ} 00'$ - $32^{\circ} 37''$ E. It occupies 25,995 square Km with a population of 369,329 (National Bureau of Statistics, 2002).

Figure 4.1 Map of Tanzania showing the location of Urambo district.



The predominant ethnic groups are mainly Nyamwezi and a few Fipa and Sukumas. Kinyamwezi is the most widely spoken language although Swahili, the national language, is also used. The main activities for the population are subsistence farming and livestock keeping. The main crops are tobacco, rice and maize. The district borders Mpanda district to the south and Kigoma rural and Kasulu districts which are also known to harbour a high number of sleeping sickness cases in recent years.

4.2.2. Data Collection

Between 2000 and 2007 only five districts in the western part of Tanzania reported sleeping sickness cases. Urambo District was purposefully selected out of the five districts, others being Kigoma rural, Kasulu, Kibondo and Mpanda, because of having the highest number of cases, and also due to the difficulties encountered in tracking sleeping sickness records in other districts. All patients recorded in Urambo district were diagnosed and treated in Kaliua Health Centre, a missionary health facility which was selected by the sleeping sickness coordinating centre in Tanzania, to manage sleeping sickness cases due to the fact that it is located in the disease catchment area, easily accessible and has proper record keeping. Relevant patient information was collected from hospital registers, for all cases diagnosed and treated in Kaliua from January 2000 to December 2007. All patient records were categorized by sex, age groups, stage of the disease, dates of admission and discharge, initial and final diagnosis; treatment provided which was done with the intention of confirming the stage of the disease, duration of hospitalization and finally the outcome of the disease. For comparison reasons, records for other diseases such as in-patient malaria, acute respiratory infections (pneumonia) and injuries were also obtained from the same registers. It was difficult to obtain stage of the disease for 22 patients diagnosed at Kaliua as the stage was not recorded in patients register and also patient case notes were not available, which would have assisted in determining the stage of the disease based on type of treatment provided. All un-staged patients recovered and were discharged from the hospital, therefore using the conservative measure that there are less non drug related complications and also no increased non drug related mortality in the early stage of the disease all the 22 patients were assumed to be early stage.

4.2.3. Data Analysis

All data were entered in Microsoft ®Excel 2003 and summarized. Population, incidences and number of deaths were summarized in age groups as follows: <1 year, 1-4, 5-9, 10-14, 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79 and 80+ years. All summarized data were entered in special spreadsheet obtained from WHO website: <http://www.who.int/evidence/>.

These were modified and fitted in stochastic model using the methods detailed in Fevre et al. (Fevre *et al.*, 2008) in order to allow capture both uncertainty and annual variability in the current estimates. Life expectancy data were obtained from the life tables' specific for African standards specific for Tanzania, also obtained from WHO website. All YLL, YLD and DALYs analysis were conducted in @ Risk software package (Palisade, Newfield, NY, USA version 5.0);

To achieve the burden of HAT calculation for Tanzania, established methods(Murray, 1994), as well as methods used in previous rhodesiense HAT estimations in Serere, Uganda (Fevre *et al.*, 2008; Odiit, 2005), were adopted and followed. To allow capture uncertainty in the current estimates, one calendar year was chosen from variability in the data obtained from 2000 to 2007.

4.2.4. Disability Adjusted Life Years (DALYs) for Rhodesiense HAT

Generally, total DALYs score for each cause-age-sex group are calculated as the sum of non-fatal burden (YLD) and the burden of premature mortality (YLL):

$$DALY = YLD + YLL$$

In order to be able to calculate a DALYs score due to *rhodesiense* sleeping sickness in Urambo, Tanzania, the methods used in the first Global Burden of Disease Study (Murray and Lopez, 1996a) as well as World Health Report (WHO, 2000) were followed. A discount rate of 3% was applied with and without age-weighting. During the DALY estimations due to sleeping sickness features such as patient's demographic data such as age and sex, severity of illness, case fatality rate, age-specific production losses and duration of disability were considered. Between 2000 and 2007, highest cases of sleeping sickness were recorded in 2004.

The population data used in the current calculations was also adjusted so as to match 2004. These were extrapolated from 2002 Tanzania population and housing census (National Bureau of Statistics, 2002) using the formula:

$$P_n = P_o (1 + r/100)^n$$

where P_n = population at time n

P_o = initial population

r = population growth rate

The population of Urambo from 2002 population and housing census was as follows:

Population: 369,329

Male: 182,393

Female: 186,936

Family size: 5.8

Growth rate: 4.8%

Households: 62,633

To achieve the calculations a stochastic model that captures uncertainty and annual variability as described in a previous documented study (Fevre *et al.*, 2008) was adopted and followed. 10000 Monte-Carlo simulations were run, the model was constructed in such a way that random sample of input values was consistently chosen for the same year data at each iteration. All output data were given in means and 95% confidence intervals.

4.2.5. Years of Life Lost (YLL)

To calculate YLL for Urambo, Global Burden of Disease recommendations were followed. Hence the used number of death were categorized in age groups as follows 0-4, 5-9, 10-14, 15-29, 30-44, 45-59, 60-69, 70-79, 80-85 and 85+.

The formula for calculating YLL using 3% discounting and uniform age weighting as given (Murray and Lopez, 1996b) is:

$$YLL = N/0.03 (1 - e^{-0.03L})$$

In the current study the formula was not used instead standard life expectancies were used. All information required to achieve the calculation are detailed in Table 4.1. Total number of both reported deaths and estimated under-reports for Tanzania (Chapter 3) of this thesis based on the rate of 0% or no under-reporting and 45% under-reporting parameters.

Table 4.1 Information required for the estimation of disability adjusted life years (DALYs) score for rhodesiense sleeping sickness.

Information type	Type of data required	Source of data used
Years of life lost (YLL)	1) Number of deaths	Health facility records of case fatality and also number of under-reporting estimates obtained from chapter three of this thesis, all these data were categorized by age and sex
	2) Life expectancy	Life tables obtained from WHO website, based on African standard life tables specific for Tanzania for the year 2004, with life expectancy at birth of 48.0 years (WHO, 200) which was assumed to be representative for the population of Urambo district for the year 2004.
	3) Distribution of deaths at birth	Health facility records, summarized for each age group (with and without age weighted case fatality rate and under-reporting rate).
Years of life lived with disability (YLD)	1) Number of cases	Health facility records and total number of unde-reporting estimated using methods detailed in chapter three.
	2) Disability weighting	from rhodesiense sleeping sickness records as per Murray (1994) methods and also using expert opinion as detailed methods in Fevre et al (2008).
	3) Duration of illness	health facility records excluding post treatment duration
	4) Age weighting of productivity	health facility records at different age groups

4.2.6. Years Lost due to Disability (YLD).

YLD are the disability component of DALYs. The basic formula for YLD is:

$$YLD = I \times DW \times L$$

Where **I** is the number of incident cases in the reference period, **DW** is the disability weight (in the range 0-1) and **L** is the average duration of disability (measured in years).

According to WHO reports clinically, *T. b. rhodesiense* is a more severe form of the disease than *T. b. gambiense* (WHO, 1998). Until recently a disability weighting 0.35 has been used in the burden of HAT estimation (Murray and Lopez, 1996a).

Recent burden of rhodesiense HAT estimates (Fevre *et al.*, 2008) recommends to use a disability weighting of 0.21 for early stage which is equivalent to malaria episode and 0.81 recommended by Murray (1994) for the late stage rhodesiense HAT as well as 0.35 in the final output so as to allow comparison.

4.2.7 Estimating Disability Adjusted Life Years in the absence of AIDS

It is known that the HIV epidemic decreased life expectancy significantly in countries of sub-Saharan Africa.

Life expectancy has a significant contribution in DALYs estimation. If it is assumed that HIV did not occur, then burden due to most of the diseases would have probably been different from what is observed today. In an attempt to compare this, it was decided to recalculate DALYs using assumption that HIV epidemic did not occur. Therefore life expectancy for the year 1990 was used for the component of estimations when HIV infection was not very severe and the results are shown in the results section.

4.2.7. Comparing relative burden of HAT and other common conditions admitted at Kaliua Health Centre

During the period between 2000 and 2007 malaria was the commonest diagnosed infection at Kaliua. However, since the highest HAT cases were recorded in 2004, relative impact of other common conditions admitted at Kaliua health centre for the year 2004 were looked at. Hence in-patient malaria, pneumonias and injuries diagnosed at Kaliua health centre in 2004 were obtained, however, in 2004 several causes of injuries were recorded at Kaliua such as burns, animal traumas, particularly attacks by lions, fractures of different bones of the body as well as head injuries of various severity caused by bicycle accidents and fall from trees, stab wounds and snake bites. Due to the fact that very few deaths due to injuries were recorded at the facility and also because all the cause of injuries have different disability weighting, DALYs estimates due to injuries were not estimated in the current study.

However, age distribution of all sleeping sickness, malaria, pneumonias and injuries recorded at Kaliua health centre were calculated and compared with the age-productivity function curve (Murray, 1994), which shows the contribution of different age groups in the society and it regards children and elderly to be less productive.

Table 4.2 Definition of disability weighting (Murray, 1994 #43)

Class	Description	weight
1	Limited ability to perform at least one activity in one of the following areas; recreation, education, procreation or occupation	0.096
2.	Limited ability to perform most activities in one of the following areas; recreation education ,procreation or occupation	0.220
3.	Limited ability to perform activities in two of the following recreation education ,procreation or occupation	0.400
4.	Limited ability to perform most activities in all of the following areas; meal preparation, shopping or housework.	0.600
5.	Needs assistance with instrumental activities of daily living such as meal preparation, shopping and housework.	0.810
6.	Needs assistance with activities of daily living such as eating, personal hygiene or toilet use.	0.920

4.2.8 Estimating the Direct Costs of Hospitalization at the Health Facility

The costs to the health system per sleeping sickness patient were estimated as the product mean hospital stay in days multiplied by a standard daily cost for hospital services. Mean hospital stay for every individual patients was calculated as the total hospital stay due to sleeping sickness divided by the number of parasitologically confirmed sleeping sickness cases at Kaliua health centre for 2004.

Based at local health facility level, a standard cost per hospital day in 2004 was estimated in terms of admission costs and initial basic laboratory investigation collected on admission to Kaliua health centre. Kaliua Health Centre being a Missionary hospital, patients are only charged a nominal amount of Tanzanian Shillings (Tshs) 1000 (approximately 1US\$), per every patient per night bed occupancy, plus a one off payment of Tshs 500 (approximately 0.5 US\$) for basic laboratory investigation on admission, the charges for all other services such as any extra laboratory investigation and treatment incurred by individual patient depending on the diagnosis and severity of condition were not included in this study.

Therefore the total costs of hospital admission and one off payment for laboratory investigations for all 143 sleeping sickness patients were estimated in order to obtain total costs of hospitalization. If it is assumed that the drugs to treat sleeping sickness were sold then, then the costs for the 30 early and 113 late stage cases were estimated and added to the costs using the rate estimated by WHO (WHO estimate cost of treatment to be US\$ 35 for early and US\$ 63 for late stage). All drugs used to treat HAT cases are provided free of charge by WHO. Ministry of Health and Social Welfare, Tanzania is responsible for ensuring smooth availability of these drugs to all treatment centres.

All other additional charges were difficult to quantify and were regarded as extra costs and were not taken into consideration, so were excluded from the current estimates as they differ according to every individual presentation. These costs include; drugs to treat all individual presentation such as fever, anaemias, pains, adverse drug events and all concomitant conditions. However, transport to and from the hospital, living costs during stay in hospital and expenses to cover living expenses for one accompanying person in hospital are regarded as indirect costs and are estimated in section 4.2.9. All sleeping sickness patients require assistance with instrumental activities of daily living such as meal preparation, shopping and housework. Total hospital stay for malaria, pneumonias, and injuries was also calculated and multiplied by standard cost for treating every individual condition. Comparisons were made to relative hospital costs of sleeping sickness cases to all the other conditions mentioned above, for which patients were admitted at Kaliua health centre.

4.2.9 Estimating the Burden of Rhodesiense HAT in Urambo in Terms of Indirect Cost to the Health System

Indirect costs in the current study were estimated in terms of transport and costs incurred by each patient during the duration of hospital stay. Costs incurred for drugs to treat other concomitant condition and additional charges were not included in this study. Data used for this part of study were collected from relatives of the patients who were admitted at Kaliua health centre during the course of the study and also patients who recovered from sleeping sickness who were visited in their homes during the case-control study which occupies the next chapter of this thesis.

Travel costs were estimated using rails costs which were assumed to be reasonable considering the fact that roads in disease endemic villages are impassable during rain season so the only reliable means of transport is through railway and all sleeping sickness villages were accessible by train.

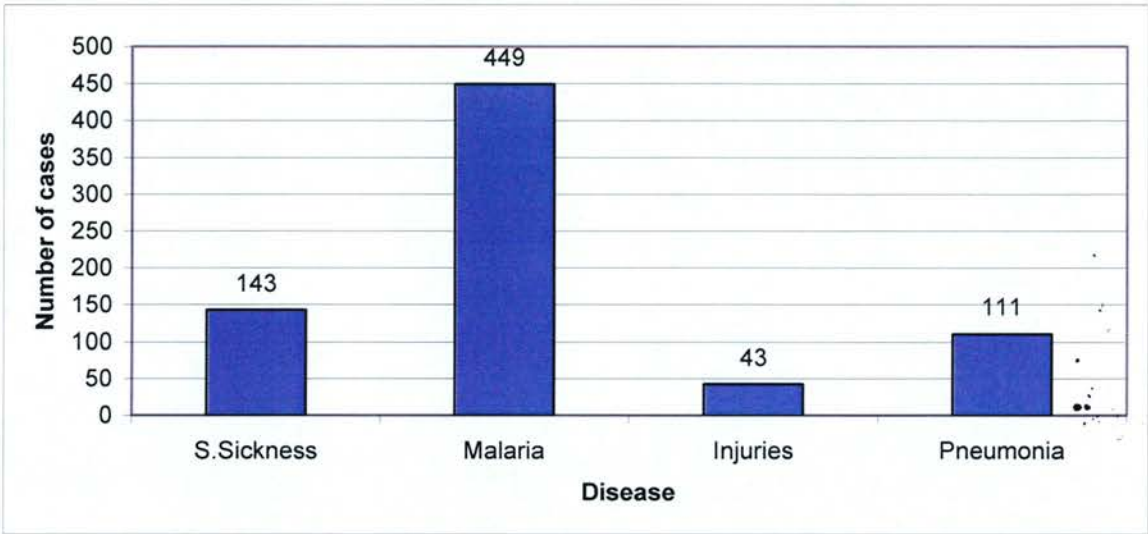
Villages for all the 143 patients, who were admitted at Kaliua health centre for the year 2004, were obtained from the hospital register. Standard travel costs were estimated based on the information provided by some of the patients and relatives who reported that they travelled in the third class train. 143 patients spent a total of Tshs 479,500.00 (approximately 479.5 US\$) on transport from their home village to Kaliua health centre. This is equivalent to 3353.15 Tshs per patient on a single trip to Kaliua. Sleeping sickness patients require assistance with food preparation and personal care, meaning all patients required one accompanying adult person (over 18 years) for the entire period they stayed in hospital. One accompanying person required an estimation of Tshs 600 per day to buy food for their patient from a local restaurant, it was estimated to cost around 100 Tshs less if food products were purchased from the local market and cooked for their patients, but this requires to have a relative or friend living near hospital where the food would be prepared, since most of the patients came from villages located far from Kaliua it was decided to estimate using modest costs of ordering food from a nearby restaurant. This was estimated at approximately 0.6 US\$ per person per day. If it is assumed that the accompanying person spent the same amount per day on meals.

The living costs for one accompanying person were estimated at the rate Tshs 500 per room per night spent in at a local guest house which was approximately US\$ 0.5. It was estimated that the accompanying person spent almost the same amount as the patient on food. Other costs such as the costs spent on general care of patient were not included in these estimates as they vary from patient to patient.

4.3 Results

Between 2000 to 2007, a total of 521 sleeping sickness cases were diagnosed and treated at Kaliua health centre as follows; 29 patients were diagnosed in 2000, 38 cases in 2001, 58 cases in 2002, 98 cases in 2003, 143 cases in 2004, 83 in 2005, 33 in 2006 and 39 cases in 2007. Highest cases of HAT were observed in 2004. Other conditions diagnosed at Kaliua for the year 2004 are shown in Figure 4.3

Figure 4.2 **Number of health condition recorded at Kaliua health centre form January to December 2004, plotted against sleeping sickness**



4.3.1. **Disability Adjusted Life Years (DALYs) score due to *Rhodesiense* sleeping sickness**

The overall DALYs burden due to rhodesiense HAT in Urambo as stated in the methodology above comprises a combination (sum) of all YLLs and YLDs estimated from the model using annual age specific data for both detected and estimated (at 0.45 (95% CI : 0.36-0.53) undetected deaths, and non age weighted discounted YLL (DYLL) are shown in Table 4.4 below. The model detected that, apart from seven deaths which were detected at Kaliua 64 (52 – 77) more cases were undetected, therefore are assumed to be unreported deaths. That is to say that for every reported death at Urambo nine more cases went unreported and died in the community.

The model also estimated that premature mortality due sleeping sickness was responsible for 190.1 (95% CI: 17.5 – 250.0) years of life if it is assumed that all cases were reported. When 45% under-reporting with age weighting and without age weighting are taken into account then sleeping sickness was responsible for 1030.5 (95% CI: 201.9-1747.3) and 610.8 (95% CI: 17.5-938.4) DALYs respectively. Table 4.4 below shows the results of years of life lost for each age group. The model also estimated that *rhodesiense* sleeping sickness was responsible for 22 (95% CI: 0-63.8) years of life lost as a result of disability in Urambo district, when no age weighting and no under-reporting was applied. When age weighting was added then the result increases to 25.5 (95% CI: 0-67.4) YLDs. A full list of age specific years lived with disability in Urambo district is shown in Table 4.5 below.

From the above YLL and YLD results if it is assumed that all sleeping sickness cases were reported and no age weighting was applied then the DALYs score for Urambo was 215.7(95% CI: 155.3 – 287.5), when age weighting is applied the result increased to 281.8 (95% CI: 209.1-362.6). If 45% under-reporting and no age weighting was applied then the result was 622.5 (95% CI: 155.3 -1095.9), however, when 45% under-reporting and age weighting is applied the DALYs score was 978.9 (95% CI: 201.9-1870.8). Age specific DALYs scores are detailed in Table 4.6 below. If disability weight of 0.35 as per Murray et al (1996) then the DALYs score was 573.5 (95% CI: 147.5-1002.1)

If it is assumed that DALYs were estimated in the absence of AIDS pandemic then DALYs score with no under-reporting would have been 205.1 (95% CI: 147.5 - 273), however, when 45% under-reporting with no age weighting was applied, then the DALYs would have increased significantly to 585.7 (95% CI: 17.5 - 1029.8) and 761.6 (209.3- 1325.3) when age weighted respectively.

Table 4.3 Years of Life Lost (YLL) due to *rhodesiense* sleeping sickness in Urambo, Tanzania.

Age of onset years	Total Population	Total annual cases	Total annual deaths	Total undetected deaths at 45%	YLLs with 45% under-reporting and		YLLs with no or (0%) under-reporting and	
					age weighting	no age weighting	age weighting	no age weighting
0-4	14,547	5	0	2.25 (1.8 - 2.7)	62.2 (0 - 146.1)	34.5 (0 - 71.1)	0	0
5-14	63,082	15	1	6.75 (5.4 - 8.1)	254.4 (201.9-338.7)	172.9 (17.5-209.3)	147.5	201.9
15-29	104,073	49	3	22.1 (17.6 - 26.5)	422.5 (0 - 804.4)	211.9 (0-368.0)	26.7 (0-60.6)	35.3 (0-79.3)
30-44	26,376	34	1	15.3 (12.2 - 18.4)	172.0 (0 - 337.5)	98.9 (0-186.8)	9.3 (0-19.5)	10.5 (0-23.8)
45-59	53,346	23	1	10.4 (8.3 - 12.4)	79.4 (0 - 154.)	58.7 (0-106.7)	3.6 (0-19.9)	3.3 (0-14.6)
60-69	11,240	9	1	4.1 (3.2 - 4.9)	26.7 (0 - 50.1)	24.4 (0-40.2)	1.1 (0-8.5)	0.7 (0-5.6)
70-79	6711	5	0	2.25 (1.8 - 2.7)	6.8 (0 - 14.9)	7.5 (0-14.4)	0	0
80+	3542	3	0	1.4 (1.1 - 1.62)	1.7 (0 - 5.5)	2.3 (0-6.8)	0	0
Total	405,636	143	7	64.4 (51.5 - 77.2)	1030.5 (201.9-1747.3)	610.8 (147.5-938.4)	190.1 (17.5-250.0)	253.9 (201.9-322.5)

All values are in mean with lower and upper 95% Confidence intervals obtained from 10000 Monte - Carlo simulations derived from the 2000 -2007 Urambo HAT data

Table 4.4: Years of Life Lived with Disability (YLD) due to rhodesiense sleeping sickness in Urambo

Age of onset (years)	Total population	Total reported cases	YLD per recovered case (early + late)	
			Non-weighted	Age-weighted
0-4	14,547	5	1.2 (0 - 6.0)	0.48 (0 - 2.37)
5-14	63,082	15	1.9 (0 - 4.2)	2.13 (0 - 4.72)
15-29	104,073	49	7.3 (0 - 15.4)	11.13 (0 - 23.24)
30-44	26,376	34	9.1 (0 - 30.6)	12.59 (0 - 42.40)
45-59	53,346	23	6.9 (0 - 22.5)	7.38 (0 - 23.87)
60-69	11,240	9	6.9 (0 - 21.9)	5.53 (0 - 17.35)
70-79	6711	5	1.4 (0 - 5.6)	0.84 (0 - 3.43)
80+	3542	3	0.9 (0 - 3.3)	0.51 (0 - 1.53)
TOTAL	405,636	143	22 (0 - 63.8)	25.55 (0 - 67.36)

Disability weights of 0.21 and 0.81 were used for both early and late stage cases in the current calculations.

The results are in mean values with 95% Confidence intervals in brackets, these were obtained from 10,000 Monte-Carlo simulations of the data derived from 2000 - 2007 Urambo sleeping sickness cases.

Table 4.5: Disability Adjusted Life Years (DALYs) due to rhodesiense sleeping sickness in Urambo, Tanzania

Age of onset (Years)	Total population	Detected cases	DALYs score no or (0%) under-reporting		DALYs with 45% under-reporting	
			age weighting	no age weighting	age weighting	no age weighting
0-4	14,547	5	0.5 (0 - 2.4)	1.2 (0 - 6.0)	61.9 (0 - 150.3)	35.1 (0 - 82.0)
5-14	63,082	15	211.4 (209.3 - 213.9)	157.2 (155.3 - 159.5)	260.7 (- 346.1)	186.0 (155.2 - 224.9)
15-29	104,073	49	51.1 (0 - 103.7)	38.5 (0 - 79.0)	46.8 (0 - 840.5)	254.2 (0 - 415.2)
30-44	26,376	34	23.8 (0 - 64.8)	19.2 (0 - 50.9)	184.6 (0 - 360.6)	117.0 (0 - 216.5)
45-59	53,346	23	10.8 (0 - 39.1)	10.7 (0 - 38.2)	86.8 (0 - 173.2)	67.4 (0 - 129.6)
60-69	11,240	9	6.2 (0 - 17.6)	8.0 (0 - 23.1)	32.2 (0 - 60.1)	31.4 (0 - 56.7)
70-79	6711	5	0.8 (0 - 3.4)	1.4 (0 - 5.6)	7.7 (0 - 16.7)	8.8 (0 - 18.6)
80+	3542	3	0.4 (0 - 1.5)	0.9 (0 - 3.3)	2.0 (0 - 5.9)	3.1 (0 - 7.6)
Total	405,636	143	281.6 (209.3 - 362.6)	215.7 (155.3 - 287.5)	978.9 (201.9 - 1870.8)	622.5 (155.3 - 1095.9)

Table 4.6: DALYs score for rhodesiense sleeping sickness in Urambo in the absence of AIDS/HIV epidemic

Age of onset (Years)	Total population	Detected cases	DALYs score with no under - reporting		DALYs with 45% under-reporting	
			age weighting	no age weighting	age weighting	no age weighting
0-4	14,547	5	0.5 (0 - 2.4)	1.2 (0 - 5.9)	41.5 (0 - 93.7)	33.8 (0 - 79.1)
5-14	63 082	15	204.1 (201.9 - 206.7)	149.4 (147.5 - 151.7)	249.3 (209.3 - 299.8)	176.8 (147.5 - 231.8)
15-29	104 073	49	48.9 (0 - 99.1)	35.9 (0 - 73.7)	335.6 (0 - 549.8)	234.6 (0 - 382.9)
30-44	26,376	34	23.1 (0 - 63.5)	18.4 (0 - 49.2)	134.8 (0 - 250.2)	108.1 (0 - 200.2)
45-59	53,346	23	10.7 (0 - 38.5)	10.5 (0 - 37.4)	61.1 (0 - 122.4)	65.7 (0 - 125.9)
60-69	11,240	9	6.2 (0 - 17.6)	8.0 (0 - 23.1)	23.0 (0 - 43.0)	31.3 (0 - 56.8)
70-79	6711	5	0.8 (0 - 3.4)	1.4 (0 - 5.6)	5.2 (0 - 11.2)	8.9 (0 - 18.8)
80+	3,542	3	0.4 (0 - 1.5)	0.9 (0 - 3.3)	1.5 (0 - 3.6)	3.2 (0 - 7.7)
Total	405, 636	143	271.8 (205.1 - 349.9)	205.1 (147.5 - 273)	761.6 (209.3 - 1325.3)	585.7 (17.5 - 1029.8)

4.3.5. Total Costs of Hospitalization for Sleeping Sickness

Between January and December 2004, 143 rhodesiense sleeping sickness cases were parasitologically confirmed at Kaliua health centre, out of them 30 cases were early while the other 113 were late stage sleeping sickness cases. These patients stayed in hospital for a total of 3601 days, resulting in mean hospital stay per patient of 25 days. The costs of hospital stay estimated for all 143 patients at the rate of Tshs 1000 (1US\$) per patient per night and one off payment of Tshs 500 (0.5 US\$) on admission were estimated at Tshs 3,672,500.00 (approximately US\$ 3672.5). If it is assumed that the costs of drugs were incurred by the patients, then 30 early stage and 113 late stage patients would have paid US\$ 1050 and 7119 respectively making a total of 11,841.5 US\$.

4.3.6. Indirect costs incurred sleeping sickness during stay in hospital

Apart from the costs incurred by every individual patient on admission costs, each patient required an additional of 63.4 US\$ which were indirect costs to cover their travel costs, meals and accommodation for one accompanying person during their 25 day stay in hospital. Other costs such as costs incurred by health providers were not estimated in this study since Kaliua is a missionary hospital and most of the care providers are based on voluntary basis. Table 4.7 shows the indirect costs as estimated for each individual patient and total cases of HAT at Kaliua.

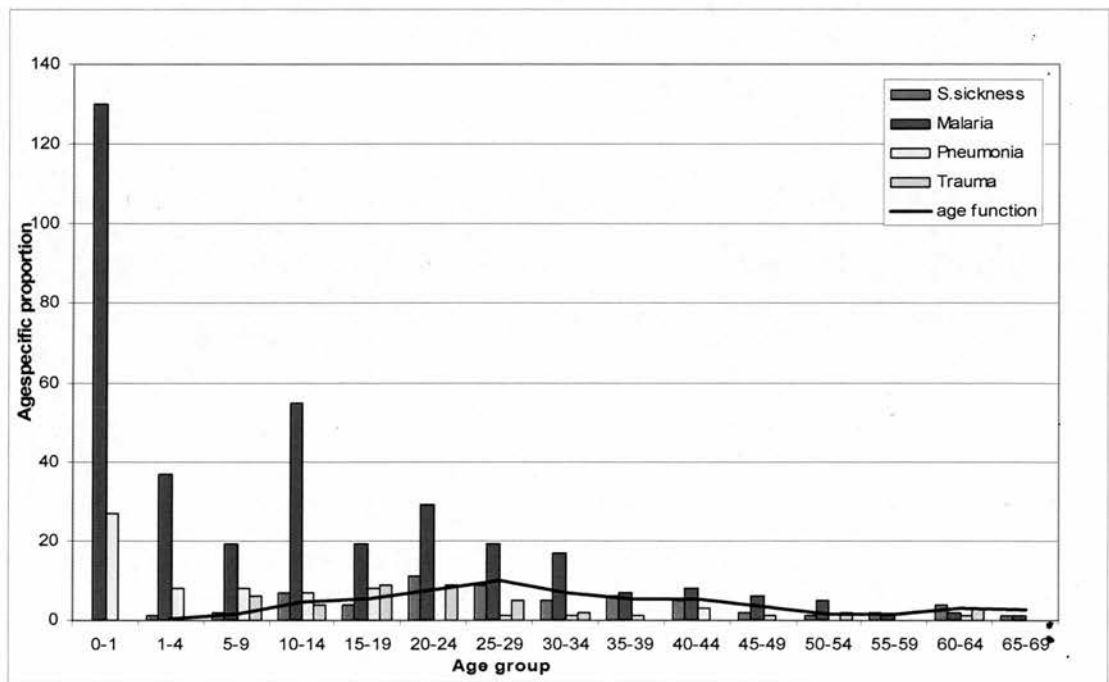
Table 4.7 Indirect cost incurred by sleeping sickness cases in health system estimated in US\$.

	Patient costs		Acompanying person costs			Total costs
	travel	meal	travel	meal	accomodation	
Costs single case	6.7	12.5	6.7	12.5	25	63.4
Total costs all cases	958.1	1787.5	958.1	1787.5	3575	9066.2

4.3.7. Relative burden of HAT compared to other diseases

In all, 449 cases of malaria, 111 cases of pneumonia, 47 cases of injuries and 143 cases of sleeping sickness were diagnosed and treated at Kaliua health centre. To compare relative impact of the four diseases, the age distribution of sleeping sickness, malaria, pneumonia and injuries admitted at Kaliua between January and December 2004 were calculated and compared with the age-productivity function curve of Murray (Murray, 1994)

Figure 4.3 Graph showing age distribution of the four diseases compared to age-productivity function curve



4.4. Discussion

Findings from the current study confirmed that the re-emergence of HAT in Urambo district continues to impose a very heavy burden to health care systems as well as

communities affected by the disease. This study utilized datasets from hospital records combined with estimates of rhodesiense sleeping sickness under-reporting in Urambo (Chapter III) which allowed an overview of populations living in rural communities to be captured. Rhodesiense HAT is severely neglected zoonotic disease, which does not appear among the top priority diseases in any of the disease endemic districts of Tanzania. This study has demonstrated how local burden can be important in prioritization of resource allocation. Existing GBD estimates for sub Saharan Africa are based on a regional model that utilized vital registration data from South Africa (Mathers *et al*, 2000) and cannot account for any local situations. Previous burden of disease studies conducted in Tanzania estimated that, Tanzania loses 10 million years of life annually through illness and death. This amounts to four months life lost per year for every man, woman and child in the country as estimated by the Tanzanian Ministry of Health (Ministry of Health, 2001). These studies also suggested that people often seek health services from more than one source, including local drug stores and sometimes traditional healers. Apparently it was observed that about 20% of the communities along the coast used no health services at all, this is a very interesting finding as communities living along the coast may be considered to have a higher level of awareness on health matters and also a better health services as compared to most of the rural communities in remote areas of Tanzania.

The current study suggested a very similar situation, as most of HAT cases presented to health facilities in late stage of the disease is probably the patients that spent most of their time seeking health support from alternative sources of health service providers, after failing to recover they decided to seek medical attention. To date, however, there is no evidence of any traditional medication used for the treatment of HAT, and also it is known that drugs used for the treatment of HAT are no longer being manufactured for commercial purposes, indicating that HAT drugs are not available in any of the drugs stores.

Findings from the current study confirmed that significantly high levels of burden are imposed on local communities are largely attributed to the HIV pandemic which severely affected most of the sub Saharan African countries. The findings suggest that if HIV/AIDS did not occur in Tanzania the burden due to HAT would have been averted by a margin of about 200 DALYs, which is a very significant figure.

The study also confirmed that communities incur very high costs to maintain their patients in the health systems. All villages from which HAT patients arise are located very far from the treatment centre. Considering the fact that HAT requires assistance with instrumental assistance such as food preparation (Murray, 1994) communities with HAT patients incur enormous costs to maintain them in hospital for prolonged duration. It's also important to note that these communities are poor and have a number of other priority health conditions to attend, including a number of other infectious diseases affecting the same families. Considering all these facts it's unlikely that these people will afford such enormous costs without any stable source of income. The majority of families in these communities live below the poverty line, studies conducted in other districts suggest that 26% of rural communities subsist on less than 1 US\$ per day during 1990-1996 (UNICEF, 1999). Besides, Tanzania has one of the lowest gross national income (GNI) per capita of sub Saharan African countries, estimated at US\$ 340 (World Bank, 2006). For rural communities to spend such huge amount of money in a single patient is obviously a serious burden.

Although this is the first attempt to estimate the burden of diseases due to rhodesiense sleeping sickness in Tanzania and the second for East Africa. Burden of other several neglected diseases and zoonoses have been estimated including the burden of rabies (Knobel *et al.*, 2005) and the burden of brucellosis (Kunda, 2006), the results of which show the similar high levels of burden imposed to health systems as well as communities.

The observation from this study shows evidence, that disease burden for individual conditions and using the local settings data which does not require much resources rather than generalizing using estimates from other areas, which in most cases may not reflect the actual situation in the affected communities. A good example of such generalization is the use of GBD estimates which were estimated using extrapolation of only 1% of South Africa data (Murray and Lopez, 1997b), which apart from not been reflective, the does not comply with the actual disease situation and mortality in other sub Saharan countries.

One of the major control challenges for HAT is the resurgence of the disease, which has been observed in many countries of sub Saharan Africa.

Some of the recent example of these resurgences have been reported in several countries (Kaare *et al.*, 2007; Kibona 2001; Moore and Richer, 2001; Van Nieuwenhove *et al.*, 2001) and there have also been reports of the occurrence of new foci of the disease in many areas of sub-Saharan Africa including Uganda and Tanzania (Enyaru *et al.*, 1999; Kibona *et al.*, 2002). There is lack of adequate knowledge regarding disease transmission and prevention among affected communities as well as policy makers (Fevre *et al.*, 2006b). There is also a lack of sufficient resources to sustain regular surveillance activities. This confirms the need for good burden of disease estimation in such communities, as it will allow proper allocation of the few available resources.

In the current study it was observed that some patients with health conditions such as pneumonia, stayed in hospital for a very short duration of time, the shortest recorded duration being two days; given the severity of the condition it is unlikely that these patients had recovered completely at the time of discharge. Two possibilities are suggested for the early discharge; one is that relatives may have requested early discharge due to financial difficulties meaning they could not afford to pay for a longer hospitalization. Second possibility is that they were misdiagnosed for pneumonia; probably they simply had upper respiratory tract infections. Tanzania

Burden of Disease Profile 2001 clearly stated that despite Health reforms in Tanzania, expecting the districts to move from managing diseases to managing health systems from a prospective of equity, the poor societies carry the heaviest burden of diseases. It is therefore difficult for any health system to target the poor accurately. However, it is possible to target the major component of the burden of disease (Grébaut *et al.*, 2004) and thus increase equity in resource allocation with more emphasis on the rural poor. For districts, this means a greater focus on cost effective interventions that address the largest shares of disease burden.

This study demonstrated that HAT imposes a very high burden on rural communities as compared to many other health conditions; this therefore stresses the need to advocate for conduction of disease specific studies particularly in rural settings.

Previous documentation suggests that most of the rural population suffers combined burden of diseases (Msamanga and Fawzi, 1997), as most of the socio-economic activities carried at the rural household level do not provide enough resource to cover health care services. Household studies conducted in Kenya and DRC have confirmed that household incomes are very limited and the cost of treatment are considered high, this can compromise the timely receipt of medical care, early diagnosis for sleeping sickness for effective treatment so as to avoid unwanted complications. It has been observed elsewhere that patients take a very long time to prepare for health care services and in most cases the preparations depend on the solidarity of the family members or even communities (Lutumba *et al.*, 2007).

The costs of managing sleeping sickness cases are very high and it is unlikely that the local communities in poor rural areas of sub-Saharan African countries will afford without support from their respective governments. This is in the context of other important priorities and serious health constraints they have to attend to. It has been observed that household members take time to prepare themselves and mobilize resources, relying on solidarity of the extended family, before they seek treatment for HAT (Lutumba *et al.*, 2007; Odiit *et al.*, 2005)

In DRC it was observed that despite acceptability of screening activity in most places, the introduction of a 'symbolic' card fee was cited to be a major obstacle for the whole exercise (Robays *et al.*, 2007), and for bigger and extended families may add one or two times a household income.

The situation may be even worse in Tanzania considering presence of a large numbers of refugee influxes from *gambiense* sleeping sickness endemic areas based in camps in the western part of the country, which pose a serious risk of introducing different species of the disease into the country. The complexity of civil instability and control of the disease have been well described in Uganda (Picozzi *et al.*, 2005). The Tanzanian study also observed that there are enormous high indirect factors attributed to this burden, such as post treatment expenses, long distance travelled by sleeping sickness patients in search for health facilities. In most cases the neighbouring health facilities may have no capacity to diagnose and treat sleeping sickness (Malele *et al.*, 2006).

It is therefore important to always incorporate the aspect of indirect expenses in burden of disease studies. It always takes HAT patients several weeks to recover fully and resume their daily productive activities.

4.5. Conclusions

Being one of the most neglected diseases, in most cases HAT is not considered an important disease in most of the affected communities as there is a tendency for policy makers to rank the disease according to their importance in the communities simply by looking on the numbers or figures. Findings from the current study have highlighted that *rhodesiense* HAT consumes a very significant proportion of workforce resource, time and hospital space. Also the results of this study demonstrated the importance of conducting disease specific burden to different common disease conditions at local settings rather than generalization using national figures.

Burden of disease due to rhodesiense sleeping sickness study conducted in Uganda recently also confirm that the outbreaks are very costly as they have focal distribution in term of time and space (Odiit, 2005). This therefore stresses the need to allocate sufficient resources towards preventing further outbreaks in these rural communities. In deciding areas that need prioritization it is important to use estimates from community perspectives rather than using health sector or national level data. Local burden of disease estimates are important aspects as they provide good epidemiological data which can be used for timely planning and proper resource allocation in most of the local health care settings, as this will contribute towards reducing greatly the burden of rhodesiense sleeping sickness.

CHAPTER FIVE:

INVESTIGATING THE RISK FACTORS FOR HUMAN AFRICAN TRYPANOSOMIASIS IN URAMBO DISTRICT

5.1 Background

Establishing the major risk factors for sleeping sickness transmission is important in understanding the nature of the disease and its transmission dynamics; this will eventually contribute greatly to an increased understanding and offer opportunities to formulate strategies for the disease control. Available documentation suggests that the disease tends to spread in previously known sleeping sickness foci and also to villages where disease has previously never been reported (Kibona 2001). However, to date not enough epidemiological documentation exists to show the patterns of disease in these areas, what might be the possible cause as well as the possible risks for transmission and maintenance.

Like many other sub Saharan Africa countries where sleeping sickness is endemic, Tanzania has shown a substantial reduction in the number of HAT cases reported between 1999 and 2006 (Simarro *et al.*, 2008). This indicates a good result of the controlled measures implemented by the Tanzanian Ministry of Health and Social Welfare (MoH&SW) and the Ministry of Livestock Development, with constant technical and financial support from World Health Organization (WHO). Among the widely used control options are medical surveillance both active and passive and control of tsetse flies (the main vector of the disease) using impregnated targets. However, despite all these tremendous control efforts made by the relevant Tanzania authorities to curb sleeping sickness and prevent further spread, it continues to be a major public health concern, particularly in the western part of the country. The situation is even more complicated with a number of issues, not least of which is the presence of substantial numbers of refugees based camps in Kigoma region in the western parts of the country, some of them originating from *T. b. gambiense* endemic regions. This therefore poses a risk of re-introducing gambiense sleeping sickness to the western part of the country where it is speculated to have occurred in the past (this is discussed in detail in Chapter II).

The western part of Tanzania is mainly occupied by agro-pastoralists who keep a variety of livestock, including domestic pigs which have also been suggested to be possible potential reservoirs for gambiense HAT, although the principal host for gambiense sleeping sickness remains to be humans (Nkinin *et al.*, 2002; Penchenier *et al.*, 1996)

Recently, a resurgence of HAT has been observed in several villages of Urambo and Mpanda districts (Kibona *et al.*, 2002). Both Urambo and Mpanda are historic sleeping sickness foci which were silent for a number of years. The districts share a common border with Kigoma region at Ugalla game reserve and are located in the western part of the country in Tabora and Rukwa regions respectively. The re-emergence was first reported in these districts early 1999, since then a number of new cases are reported to Ministry of health every year. Between January 2000 and December, 2006 a total of 446 cases were recorded. The most common vectors associated with the current re-emergence in Urambo are mostly *Glossina morsitans* (MoH report, 2004) It is estimated that 60-70% of the country is infested with tsetse flies (Kihamia *et al.*, 1991).

In 2005, in response to the existing resurgence, the Ministry of Livestock Development deployed a number of insecticide impregnated targets in most of the endemic villages of Urambo district. The impact of this effort reduced the number of cases to 85 in 2005, and 33 in 2006. All these cases were diagnosed and treated at the Kaliua health centre, in Urambo district, which acts as HAT treatment centre for the district. The health centre, was also receiving patients from neighbouring Kigoma rural and Mpanda districts until mid 2005. However, Mpanda district then started receiving supplies of drugs for the treatment of rhodesiense sleeping sickness resulting in less need for sick patients to travel to Kaliua in search of treatment for HAT (Annual Report, 2005).

Much is already known regarding sleeping sickness in other sub Saharan African countries where the disease is endemic.

Despite the existing disease challenge and also concern expressed by some authors about the challenge ahead by comparing the current resurgence with the epidemics of 1930s (Nkinin *et al.*, 2002), in Tanzania little has been achieved in terms of understanding the epidemiological dynamics of the disease in all affected areas. There still exist many unaddressed gaps, such as identifying the source of infection and possible factors exposing people to disease risk which must be dealt with before we can predict the future outcome of the disease in all the affected districts. There is an urgent need to investigate properly the factors which may have contributed towards the current resurgence of the disease in the district as well as the occurrence of new foci in Tanzania. In dealing with this issue, involvement of all stakeholders responsible for human health, vectors and reservoir hosts are essential.

Though it is known that spatial distribution of vector-borne diseases is demarcated by the geographical distribution of vectors and their vertebrate hosts, there is always a tendency to use political boundaries to investigate the disease processes in both epidemiological as well as in daily public health surveillance systems. In opposing this tendency (Cattand *et al.*, 2001) recommended the use of village and hamlets as the most appropriate reporting units for sleeping sickness. Despite the wide spread use and potential benefits of geographical information systems in epidemiological studies, there are so far no or very limited documentation to show its use in studies conducted in Tanzania to investigate the spatial distribution of sleeping sickness.

There is always an increased benefit using multiple techniques in the disease investigation, as they may provide potential information which may contribute toward designing better options for disease control. Higgs *et al* (2001) recommends the use of GIS in targeting resources for disease prevention by highlighting areas of significantly high rates and to predict areas for future risk (Higgs and Gould, 2001).

Hence adding GIS analysis in epidemiological studies may play an important role in the assessment of geographical patterns of the disease in order to detect unusual spatial aggregations of the disease incidence or clusters.

5.1.1 Case Control Studies

Case control studies are studies whereby researchers compare medical and lifestyle histories among two groups of people with similar settings: those with the disease or health condition under study and a similar group of people without the disease or health condition. The aim of such studies is normally to establish the association of the established factors with the health condition among these two groups of people.

There are some documented case control studies for HAT which were conducted in other endemic countries. These are important to review when conducting studies of responsible factors for the resurgence of sleeping sickness in Urambo. A study on gambiense HAT conducted in Ivory Coast (Meda *et al.*, 1993) observed that people sleeping in farms (encampments) and people fetching water in natural holes and pools were more likely to become infected than those living at the village. In Busoga Uganda (Okia *et al.*, 1994) found that spending more time outside the village of residence, visiting areas where rhodesiense sleeping sickness is endemic, collecting firewood in the forest and having incidents of sleeping sickness in the family were observed to be significantly associated with the risk of acquiring sleeping sickness. Another case control study conducted in a gambiense area in Cameroon found that hunting was a risk factor for sleeping sickness (Grebaut, 2001). Recently several risk factor studies were conducted in a rhodesiense HAT area in Uganda. In the first study Odiit *et al* (2006) used remote sensing and GIS to detect villages of high risk, they also observed that distance to sleeping sickness hospital, long vegetation swampland and low population density influence the population of tsetse flies and hence were predictive of reported sleeping sickness presence (Odiit *et al.*, 2006).

In another study highlighted the importance of considering animal movement as an important risk for zoonotic infections, and finally (Zoller *et al.*, 2008) observed that having a family member with a history of HAT as well as proximity of a homestead to a nearby wetland to be strong risk factors for infection. However, in Tanzania, no risk factor studies for HAT have been conducted in any of the disease endemic areas, although several suggestions have been put forward as the possible factors which were likely to expose residence of disease endemic areas to the risk of infection. Kilama (1981) reviewed the relationship between human activities and trypanosomiasis over ten years (1970 to 1980) and suggested that farming, clearing the land for the purpose of establishing new home, fetching water, travelling, collecting building materials and honey collection as the most important activities exposing human population to tsetse contact (Kilama, 1981). This study aimed to investigate the risk factors associated with sleeping sickness transmission in Urambo district through a matched case-control study. The above factors were also considered during the study design.

5.2 Material and Methods

5.2.1 Description of the Study Sites

5.2.1.1 Study area

The study was conducted in Urambo district, which is located in Tabora region in the western part of Tanzania. The district was established on the 1st July 1975 and it is the largest out of the six districts in the region. It lies 1,100m above sea level, between latitude 40°00" and 50°00" south and longitude 30°00' and 32°00' east. Urambo has a total area of 25,995. km². Out of these 2,859.45 (11%) km² are used for settlement and agriculture activities and 23,135.55 km² (89%) is covered by forest, bush and water bodies. The district has a warm climate, which reaches a peak in August-October with a mean daily temperature of 21.5 – 27.0°C. May to July are cooler months, followed by dry a period of dry wind which last up to September.

The only rainy season in the district starts from November lasting to May and the total annual rainfall varies from 900 mm to 1,300 mm.

The district comprises four administrative divisions, 23 wards and 108 villages which includes 97 residential villages and 11 villages which are occupied by refugees.

5.2.1.2 Agro – economic zones

Urambo has relatively homogeneous topography and temperature with two agro-economic zones; the Western and Miombo zones. The western zone in which the study was conducted is sparsely populated and varies in elevation ranging from 1000 – 1500 m. It is characterized by flat and featureless topography with area sloping away to the rivers Ugalla, Malagarasi and Lake Sagara to the west and south. The district produces both cash and subsistence crops including tobacco, maize, cassava and beans, with paddy grown in depressions or wet areas.

5.2.1.3 Livestock development

Despite the district having the richest potential of grazing land the amount of livestock kept in the district is very low. One of the factors limiting livestock keeping is tsetse fly infestation. Livestock diseases in the district are quite a problem which leads to poor livestock health and even death. The short horn Zebu is the predominant breed of the indigenous livestock, which means low herd productivity. The most important cattle diseases in the district are tick borne diseases namely East Coast fever (ECF), *Anaplasmosis*, *Babesiosis* and Heart Water followed by contagious bovine Pleuropneumonia, *Trypanosomiasis* and skin diseases. Evidence of the actual tsetse infestation situation in disease endemic villages in Urambo is as seen in Figure 5.1.

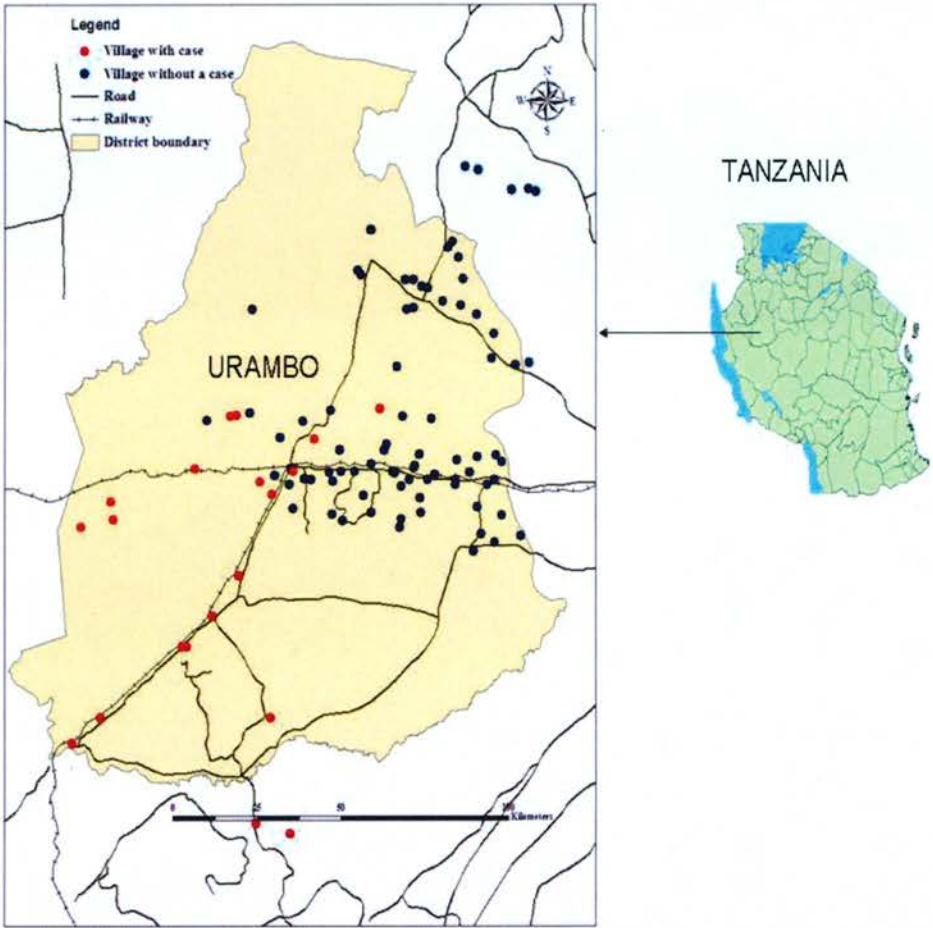
Figure 5.1 Tsetse fly infestation as captured on the main route between Usinga to Ukumbikakoko



5.2.1.4 Study population

According to the 2002 population and housing census 2002, Urambo district had a population of 370,796. With the annual growth rate of 3.6%, the district population was projected to be 471,143 at the end of 2007 (National Bureau of Statistics, 2002). The predominant indigenous tribe of the district are Nyamwezi followed by the related Sukuma. Significant minorities include the Ha who originate from Kigoma. In recent years refugees from Burundi have added variety to the district ethnic make up.

Figure 5.2 Urambo map showing location of all villages; sleeping sickness villages are marked in red and the village without disease in blue



5.2.2 Study design

The design of this study was matched case-control (Woodland, 1999), investigating risk factors for rhodesiense HAT in Urambo. Two stages of the study were conducted by investigation of the risk factors at both village as well as within village level scales.

5.2.2.1 Village level survey

This study was carried out to examine village-level risk factors, involved detailed mapping of all 108 villages in the district. The aim of this kind of spatial study was to explore the possibility of having disease clustering in the district.

All villages as well as health facilities in the district were surveyed and geo-referenced using GPS. During this survey information regarding whether sleeping sickness has ever been reported in the village was gathered from the clinical staff. The aim of collecting such information was an attempt to validate the information obtained from the district hospital. The information collected at the health facility level included previous number of sleeping sickness cases. This was done concurrently with the mapping exercise of all village centroids as well as all the health facilities in the district. For this particular study the village reference point for mapping was taken as the common meeting point in the village. This stage also included collection of all geographical information which was considered to be related to sleeping sickness in the area, such as location of livestock markets, watering points (rivers, lakes and wells) and swamps.

5.2.2.2 The Within Village Survey Risk Factors

The within village level survey was sub-divided into two parts as follows:

The first part which aimed at exploring the possibility of disease clustering within the village included total mapping of all homestead in six selected disease endemic villages. A criterion for selecting the six villages was to have five or more sleeping sickness cases, recorded between 1st January 2004 and 31st July 2007. All homesteads in these villages were mapped entirely using hand held Geographical Positioning System (GPS). The reference point for the homestead was taken on the front door of every surveyed household.

The second part of the within village survey aimed at investigating the behavioural risk factors for sleeping sickness using structured questionnaire to all sleeping sickness cases identified during this exercise, as well as the matching controls.

5.2.2.3 Behavioural Risk Factor for Sleeping Sickness in the Villages

Between January 2004 and July 2007, when the study was conducted, a total of 21 villages reported sleeping sickness in Urambo district

A list of names of all sleeping sickness patients from these villages was obtained from both Urambo district hospital as well as Kaliua health centre. Six villages with the highest number of cases (five or more) were selected from the list and visited. All cases were traced back to their respective villages, where age and sex matching controls were randomly recruited. Interviews using structured questionnaire were conducted to both cases and controls, in addition all homesteads for cases and controls were geo-referenced. Detailed techniques used for the recruitment of cases and their matching controls are explained in sections 5.2.7.2 and 5.2.7.3 respectively, and the questionnaire used is attached in appendix 5.

5.2.3 Study Sample Size.

Win Episcopo 2.0 (Thrusfield *et al.*, 2001) was used to estimate the sample for the study. The target was to enrol a minimum of **96** cases and a minimum of **96** matched controls during the period of the study. With this sample size the intention was to have 80% (alpha error 5%) to detect risk factor with odd ratio of 3 that was assumed to be present in at least 10% of the non-exposed, assuming a phi-coefficient up to 0.2 (Dupont, 1988).

5.2.3.1 Recruitment of Cases

We define a case for this particular study as a “person who presented at any health facility between January 2004 and July 2007 to seek treatment and who was diagnosed to have sleeping sickness”. Criteria for inclusion in this study was first to be parasitologically confirmed as having sleeping sickness, using WHO criteria for diagnosis of sleeping sickness. The criteria include; demonstration of trypanosomes in the blood, gland aspirate or lymph for early and demonstration of parasites in the CSF, WBC $>5 \text{ mm}^3$ for late stage. A second criterion was to be residing from Urambo district and having lived in the village for more than two years.

All sleeping sickness cases which matched the criteria were followed to their respective villages. At the village a brief meeting was held between the research team and village health team. The village health team comprises one of the village leaders, a chairman, village executive officer (VEO) or both, a medical expert from the village health facility if any and two other key members chosen from the community members in most cases these were influential people in the catchment area preferably the members of village health, agricultural or educational expert or tsetse officers or any other member chosen by the village team. The aim of the meeting was first to introduce the research team and explain the purpose of the study and secondly to seek permission to conduct the study in the respective village. After obtaining consent for the study, the village level questionnaire was then administered immediately. The list was produced and village leaders were requested to locate homesteads for all the cases arising from their respective areas.

All cases were traced and interviews were conducted, at the same time their homesteads were assessed and geo-referenced. In situations where interviews were conducted away from case homes, subjects were requested to show the researcher their homestead where the mapping exercise was done as well as assessment of the household.

To avoid duplication in the mapping, the names of head of all households were recorded and also the number matching the list and date of the interview was marked on the front door of the homestead using a chalk. This was done to avoid confusion in situation where two or more people bare similar names.

5.2.3.2 Recruitment of controls

A control for this study was defined as “a person not diagnosed with sleeping sickness, and had lived in Urambo district for the same period of two years.” This control age and sex matching each case was randomly selected from the same village population. Using the list of villages which reported sleeping sickness obtained from the district hospital, villages were visited. At the village level, a brief meeting was held between the research team and the team of village leaders.

During this meeting a village chairman or village executive officer (VEO) was requested to provide a list of all ten cell unit¹ leaders in their respective village. At the ten cell level, a list of members of all household in the respective ten cell units was produced, member listed by number from one to ten. Without looking at the list a random village member was requested to mention any number starting from one to the last number of our ten cell list. The household matching this number was selected from the list and the ten cell leader was requested to provide the names, sex and age of residents of the selected household, a control age sex matching the case of interest was picked from the household. In case no control was found from the selected household, then another number was picked using similar procedures until the required control was obtained.

In selecting the matching controls ten years age range was allowed so as to avoid any possibility of missing a control matching the exact age, and assuming that at that age range most of the community members share

¹ A ten cell unit is the smallest village level administrative unit, and it normally comprises of ten families (homesteads), in very rare cases more than ten families but less than twenty.

similar risk activities. The minimum age for this particular study was 10 years. Hence the age-group which was considered in selecting the potential controls followed the following range (10 - 19, 20 - 29, 30 - 39, 40 - 49, 50 - 59, 60 - 69, 70 - 79, 80 - 89, 90+). In situations where the control matching the case was not found in the visited household or if the control refuses to participate in our study, then another household was randomly selected from the same ten cell unit using the same techniques, and in situation where no suitable control was obtained from the visited ten cell unit then the research team selected another ten cell unit until the suitable control was obtained. The control was only included in the study after verification that the household consists of hospital attendees (i.e. population who would present to the health facility if suffering from any health condition). Once a potential control was identified, the purpose of the study was explained, and they were interviewed only if they agreed to participate and they had been residents of the Urambo district for two or more years.

5.2.3.3 Household Surveys

Based on previous case control studies the questionnaire was structured to gather information on a range of variable related to individual and household behavioural characteristics such as socio-economical and daily household activities, movement or travel history and a range of all possible risk activities which expose an individual to tsetse fly bite such as farming, honey gathering, lumbering, firewood collection, fishing, heading livestock, hunting and business. The questionnaire used for this study can be found in appendix 5. During the interview detailed assessment of economical status of the selected homestead was carried out. This included a range of factors such as structure and roofing of the house, number of rooms, and type of toilet, size of the family. The questionnaire also investigated types of crops grown by the family members and area where the farming was conducted, type and amount of livestock kept by each family, as well as other sources of household income. It also investigated the possibilities of contact with wild animals in the village. The interview was recalled for the risk period i.e. during the time when a matching case was infected. The questionnaire

underwent two rounds of pre-testing, first round it was pre-tested among the colleagues at the University of Edinburgh so as to avoid any ambiguity in the questions and the second round it was pretested in the field in sleeping sickness endemic area in Tanzania, which was outside the study villages.

5.2.4 Keys Informants

During our study in-depth discussion was held between principal research team and village local leaders (village/sub-village) team which included a team of influential people from the village, health/veterinary/agriculture board members, livestock keepers, the aim of this meeting was to gather information on land use practices, livestock keeping grazing, watering points, cattle marketing centres and livestock routes.

5.2.5 Data processing and statistical analysis

Data processing was subdivided in the sub-section depending on the means of data collection.

5.2.5.1 Geographical Information System

An in depth study of HAT in the study area requires a clear demarcation of different ecological zones in and around the district, during this study spatial data (geographical coordinates) of the residence of each cases and controls (i.e. geo-referencing exact point locations of all homesteads in the villages of active sleeping sickness cases) as well as mapping of location of kraal (if any) in all homesteads, location of health facilities, village centres was recorded using GPS. All the coordinates were compiled using Microsoft Excel where were converted in Dbase IV, then imported into ArcView

software which was used to convert them into a point map using Arc view version 3.2 software. All maps in this chapter were conducted in ArcGIS 9.1 software. Spatial data were analysed using SaTScan software, which is freely downloadable from the internet at <http://www.satscan.org>. SaTScan is based on Kulldorff's spatial scan statistic (Kulldorff, 1997).

The SaTScan statistics which were used in the current study are space scan statistics and are useful for the use in areas as well as point data. It can utilize a Poisson-based model as well as Bernoulli based model. The first model requires the number of events in an area which are Poisson distributed under the null hypothesis, whereas the later model requires events data such as cases and controls. Therefore the Bernoulli model was used in the current analysis.

The spatial scan statistics is a local cluster test which detects the location of the most likely cluster of events in a data set, and infers its statistical significance using Monte Carlo replications. Grid points, (referred to as centroids) are superimposed on top of the sampling area. Around each centroid, circular zones with a continuous varying radius are constructed. The likelihood test ratio statistics for each zone, which is based on the population and the number of cases included within that zone is calculated. The total number of zones around each centroid, although infinite in theory due to the continuous variation of the radius, is in fact limited by the possible combinations of population and case numbers. Usually the zones are restricted in size to include a maximum of 50% of the population, as high rate clusters larger than this signify a cluster of unusually low rates of events in the remaining population. The program is also capable of reporting secondary clusters, which are all other clusters which do not overlap the most-likely cluster. This occurs if the likelihood ratio is larger than the likelihood ratio for the most-likely cluster for at least one data set simulated under the null hypothesis.

5.2.5.2 Cluster detection

In order to investigate the spatial distribution of rhodesiense HAT in Urambo, two levels of analysis carried out: The first part which was the village level cluster analysis, included all the 21 villages which reported sleeping sickness between January 2004 and July 2007. These 21 villages were categorized as case villages regardless the number of cases reported per village, the remaining 87 villages which did not report sleeping sickness were categorized as the control villages. The second part of cluster analysis is within village study, in this part the six villages with five or more cases were chosen and surveyed. All homesteads in these six villages were surveyed and mapped entirely. Homes with sleeping sickness cases were categorized as case homesteads, while homes without sleeping sickness reports within study time frame were categorized as control homesteads. All spatial data were entered in Microsoft ® Excel software where it was converted into text files and then imported into SatScan software version 7.0.3 (Kulldorff, 1997; Kulldorff and Nagarwalla, 1995). In the Sat Scan software 50% was set as the maximum cluster size for total population at risk, the analysis was run to identify areas of high rates clustering (Kulldorff, 1998) rather than low rate clustering. The analysis was set to run with 999 Monte-Carlo iterations.

5.2.5.3 Hard copy Maps

Maps used in this chapter were reproduced using the geographical information system, ArcView and ArcMap9 (ArcGis 9, ESRI Systems, Redlands, CA, USA).

5.2.5.4 Questionnaire data

Individual data was digitized using database software, Microsoft Access (Microsoft Office XP, Redmond, USA) and transferred to Microsoft Excel spreadsheet (Microsoft Office XP, Redmond, USA) where it was stored as comma delimited (csv) files.

It was then imported to R package (R: copyright 2004, The R foundation for Statistical Computing Version 2.7.1, available free on the internet at <http://CRAN.Rproject.org> ready for analysis) to summarize the characteristics of cases and controls (Table 5.1).

Cases and controls were 1:1 matched and compared using a logistic regression to determine the risk factors associated with Rhodesiense sleeping sickness as a univariate analysis (R-commands are shown in Figure 5.3.1). All individual variables were examined for each of the village variables separately. Both individual and village characteristics were treated as fixed effects. For this analysis, a generalized linear model (GLM) with binomial errors (Crawley, 2002) was used with R 2.7.1 to calculate the odds ratios (OR), 95% confidence intervals (CI) and p-values for statistical significance ($P < 0.05$).

Figure 5.3 Example of R command used in the current analysis

```
>clogit (CC~SSinFamily+strata(CCRrefNo.),data=CaseCont)
```

As a multi-variate analysis, logistic regression using a GLM with binomial errors was performed for the factors that had a $P < 0.2$) at the univariate level. Variables were removed from the model using backward stepwise model simplification (Crawley) until all terms remaining in the model were significant ($P < 0.05$). Figure 5.3 is the example of the commands used, and the results of this multivariate analyse are shown in Table 5.4.

Figure 5.4 R commands used in multivariate analysis of this study

```
>lModel<glm(Case.Control~ForestVisit+SSinFamily+AreaVisit+SeeLion+
SeeHyena+SeeElpnts+SeeMntlzd+SeeWrthgs+SeeRats,family="binomial")
```

The GLM for the multivariate analysis identified single significant risk factor: having a member of family with previous sleeping sickness history (Odds ratio: 20.69 (95% CI: 4.79 – 89.33), $P < 0.001$, Table 5.5). All other factors which were initially significant turned out to be insignificant in this model. The codes used to obtain the odds ratio and 95% confidence intervals are shown in Figure 5.5.

Figure 5.5 Example of the codes used to obtain the odds ratio and 95% Confidence interval in the multivariate analysis

```
odds<-exp(coef(summary(model))[,1])

lower<-exp(coef(summary(model))[,1]-1.96*coef(summary(model))[,2])

upper<-exp(coef(summary(model))[,1]+1.96*coef(summary(model))[,2])
```

5.3 Results

5.3.1 Village Level Spatial Results

The first part of the study aimed to investigate the possibility of sleeping sickness clustering at the village level in Urambo district. Twenty one sleeping sickness case villages and 87 control villages were included in the analysis of this first part Findings of the analysis demonstrated significant clustering ($P < 0.001$) with a radius 82.88 km, in the district. Table 5.1.below shows the results of the model output. It also shows that 17 out of 108 villages were the most likely clustered sleeping sickness villages in the district. These included; Ukumbikakoko, Usinge, Lumbe, Ukumbisiganga, Kangeme, Zugimlole, Maboha, Ulindwanoni, West Kaliua, Tuombemungu, Ulindwanoni, Limbula, Imalampaka, Luhanjo, Shella, Kamsekwa and Kombe.

5.3.2 Within the Village Spatial Analysis Results

The second section of this part of the study aimed at investigating the possibility of clustering within the village, six villages with five or more cases were chosen and total mapping of all homesteads was conducted. Location of all case homesteads in each village was identified. Non-case homestead data were entered in SaTScan software for analysis as village controls. (Table 5.2).

The model also suggests a small secondary cluster involving only two villages which are Kazanaupate and Mtakuja, both in Igagala ward which was statistically insignificant ($P = 0.955$).

Figure 5. 6 Insectside impregnated target as photographed on the borders of Usinga and Ukumbikakoko villages



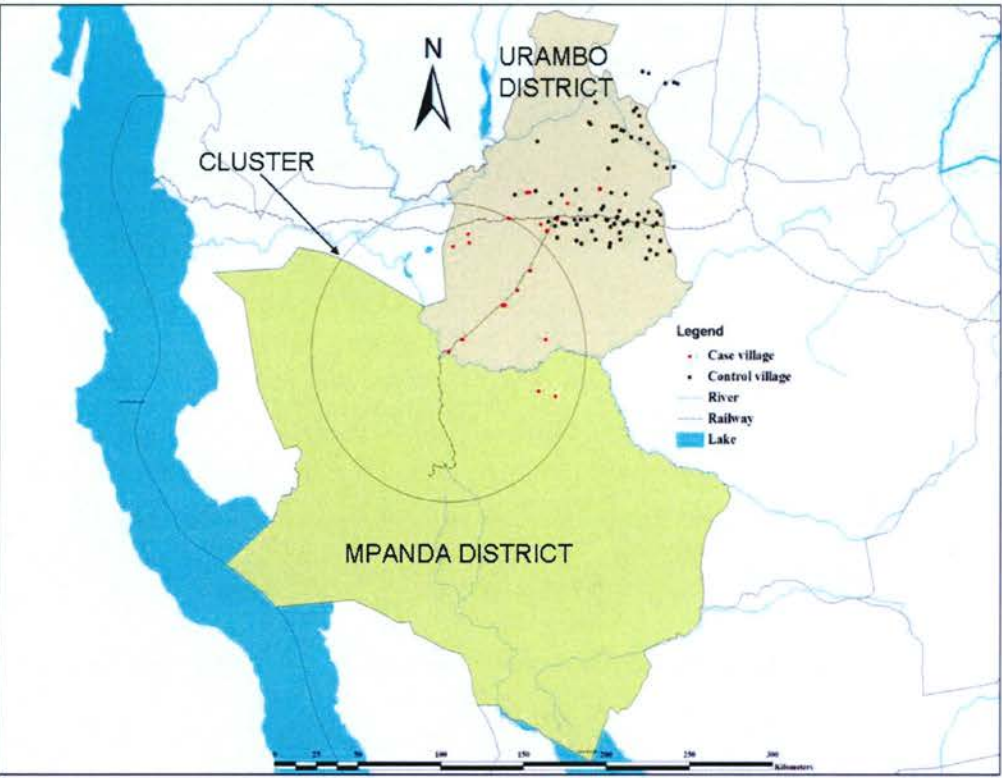
Table 5.1 Results of spatial analysis at the village level

Type of cluster	Number of cases	Location of cluster (Coordinates)		Radius (km)	Expected cases	Rate Ratio (Obs/Exp)	Relative risk	Log likelihood ratio	Monte Carlo rank	P - Value
		X	Y							
Primary	20	31.206750	-5.731540	90.10	3.15	5.082	21.412	31.537649	1/1000	0.001
Secondary	20	31.630220	-4.932450	1.64	0.37	5.400	5.889	3.457675	955/1000	0.955

Table 5.2: Spatial results at individual village (within the village level) in Urambo district.

Village	Number of Location of cluster (Coordinates)		Radius (km)	Expected cases	Rate Ratio (Obs/Exp)	Relative risk	Log likelihood ratio	Monte Carlo rank	P - Value	
	cases	X	Y							
Lumbe	36	-5.500870 -5.501060	31.499040 31.494870	0.22 0.00	13.90 0.17	1.798 12.083	3.612 12.735	7.652848 5.035663	109/1000 917/1000	0.109 0.917
Ukumbisiganga	18	-5.495810 -5.498290 -5.497510 -5.500730	31.516540 31.512630 31.511710 31.514740	0.05 0.09 22.83 0.05	0.33 0.80 0.18 0.22	9.667 5.012 11.278 9.022	11.400 6.159 12.562 10.025	4.974151 3.896307 3.650935 3.099132	686/1000 915/1000 970/1000 997/1000	0.686 0.915 0.97 0.997
Usinga	7	-5.670190	31.282170	0.06	0.54	7.377	15.879	6.388538	74/1000	0.074
Ukumbikakoko	5	-5.738090 -5.732600	31.211220 31.201900	0.10 0.52	0.19 0.62	10.800 3.240	17.333 4.733	4.142072 1.335523	421/1000 935/1000	0.421 0.935
Kangeme	25	-5.424530 -5.427400 -5.426690	31.576930 31.577740 31.580280	0.02 0.02 0.02	0.10 0.10 0.15	19.400 19.400 12.993	21.000 21.000 13.971	6.008640 6.008640 4.147939	625/1000 625/1000 941/1000	0.625 0.625 0.941
Kombe	6	-5.045210 -5.061260	41.562670 31.531620	3.12 0.07	0.27 0.18	11.167 11.167	21.333 16.250	5.797100 3.654219	216/1000 666/1000	0.216 0.666

Figure 5.7 Urambo map highlighting all high risk villages which are included in the cluster

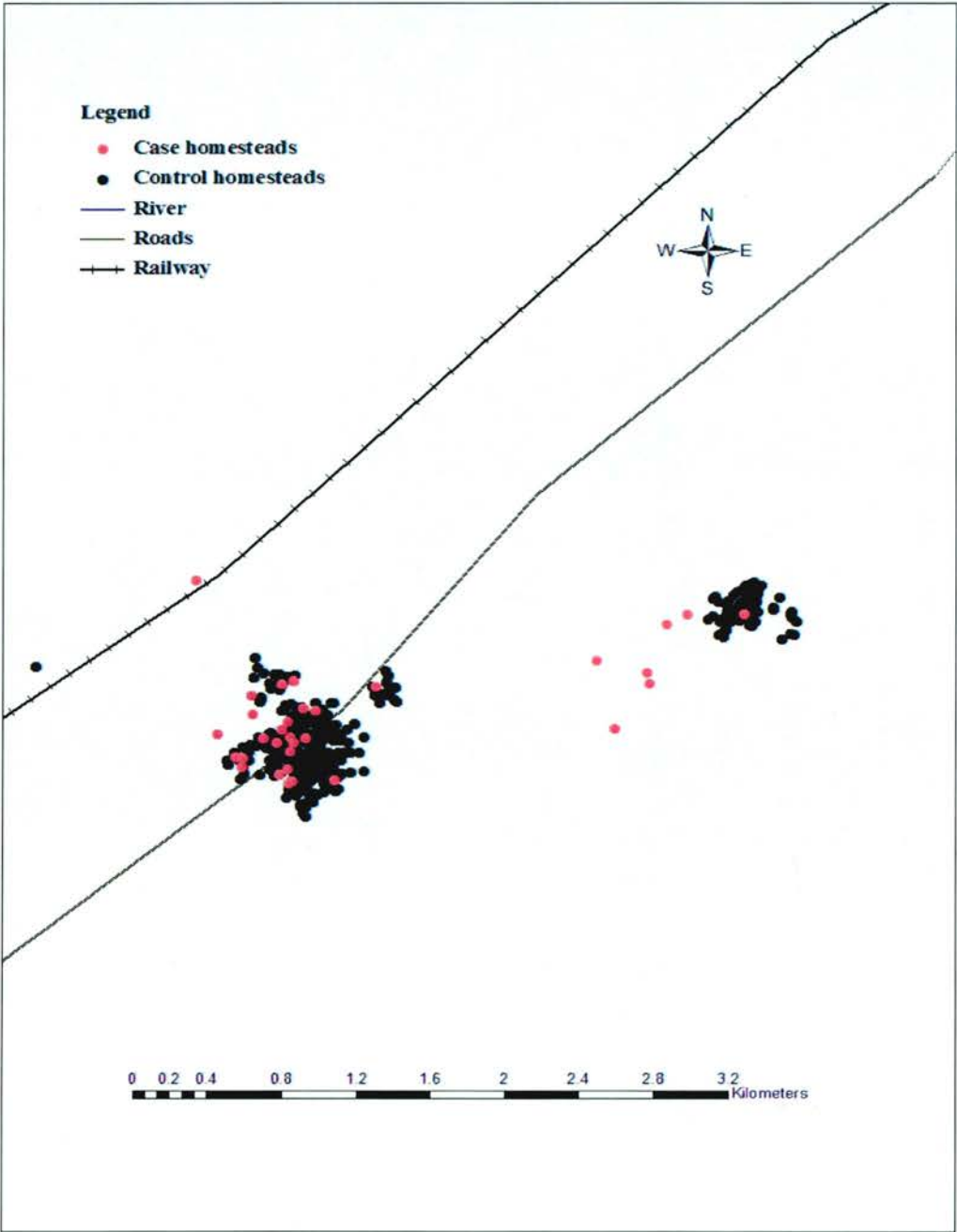


5.3.2.1 Lumbe Village

During review of hospital records 56 sleeping sickness patients from Lumbe were diagnosed and treated at Kaliua health centre between January 2004 and July 2007. However, the current survey discovered only 36 cases out of the 56 recorded came from Lumbe, 18 patients out of the 56 which were originally reported under Lumbe were found in Ukumbisiganga which is very close to Lumbe. Two cases could not be traced. We mapped 431 homesteads in Lumbe using GPS; out of these 36 were case homesteads and the remaining 395 were entered in the analysis as control homesteads. The results of the Lumbe village analysis suggested clustering ($P = 0.109$) but was not statistically significant.

The map showing the distribution of all case and control homesteads which were included in the analysis is displayed in (Figure 5.8).

Figure 5.8 Lumbe map showing the distribution of homesteads with cases as well as all households without cases.

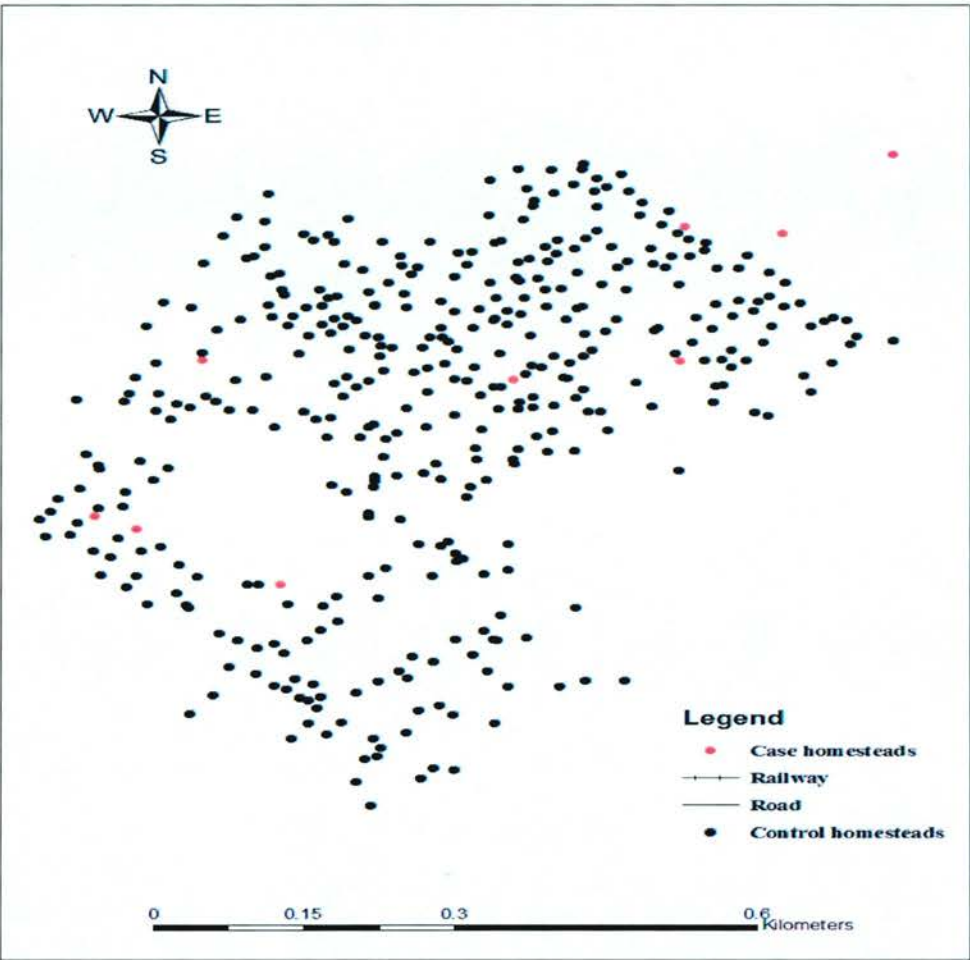


5.3.2.2 Ukumbisiganga Village

Data collected from district hospital did not report Ukumbisiganga as a village; instead it was reported under Lumbe. Originally these were known as one village under the name Lumbe or “Kilometa sitini” in Swahili (meaning 60 Km) this is the distance measured when travelling by train.

During the survey it was realized that 18 sleeping sickness cases reported under Lumbe were in fact from Ukumbisiganga. In total, 406 homesteads (18 sleeping sickness cases and 388 village controls) were surveyed and mapped in Ukumbisiganga for the analysis. Findings from the analysis suggested there was most likely a cluster ($P = 0.69$), relative risk 11.4, radius 0.05, rate ratio (O/E) = 9.667 and Log likelihood ration 4.97. However, statistically there was no association. Figure 5.9 shows the homogenous distribution of all these cases of sleeping sickness as well as the village controls.

Figure 5.9 Ukumbisiganga map showing the location of all case and control homesteads.

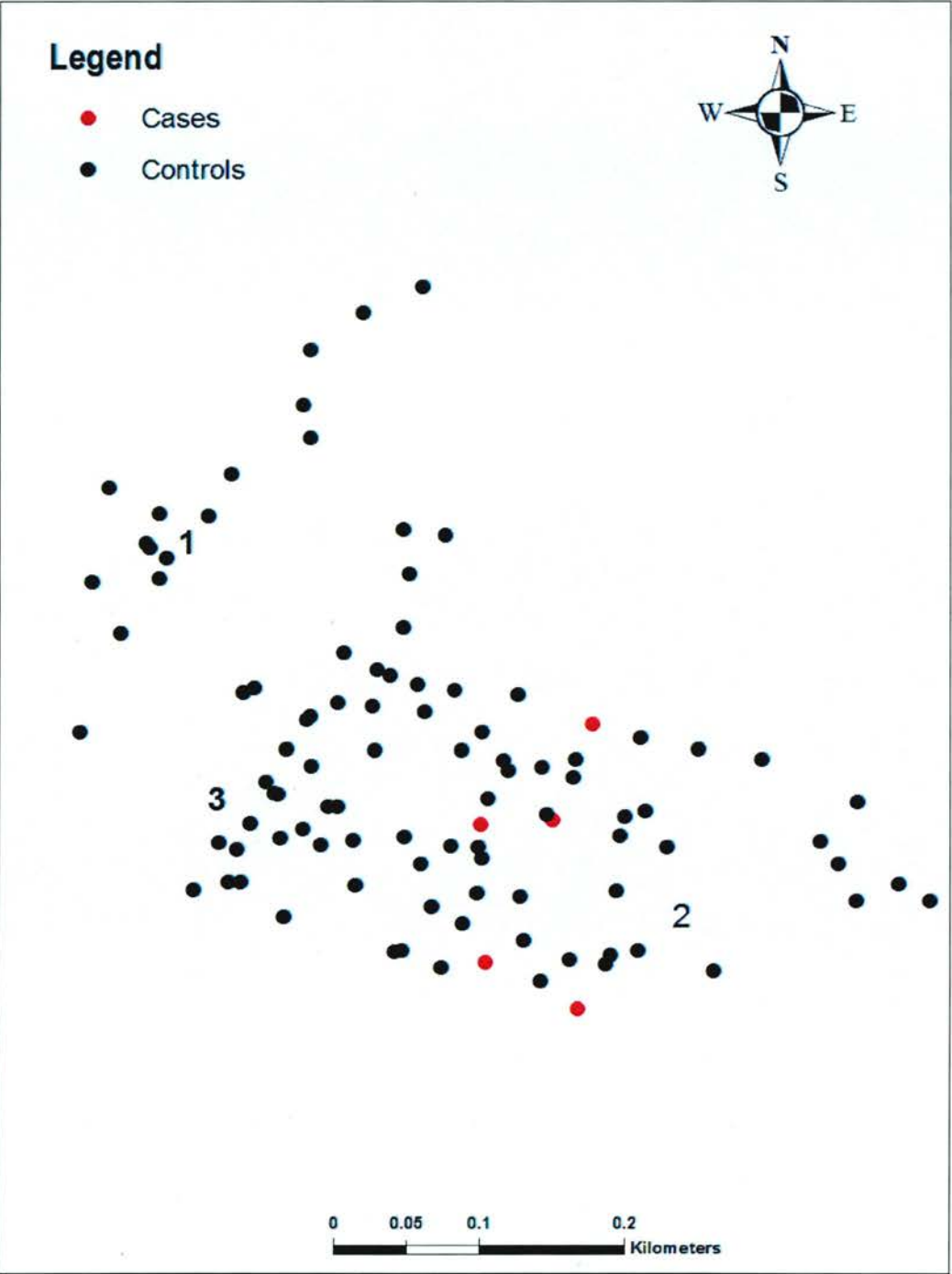


5.3.2.3 Usinga Village

Ten cases of sleeping sickness for Usinga were obtained from the hospital records; Usinga was different from the previous two villages due to the fact that it is more remote, though it may not differ much in size from the other villages. It is less populated and many of its residents live inside the forest reserve. Accessing this village one has to travel a long distance through a dense forest on a very narrow road which is heavily tsetse infested (picture in Figure 5.7). There is also an increased danger of wild animals in Usinga when compared to other villages. A small sub-village of Usinga called Kasense (No. 3 Figure 4.5) is located on the shores of River Ugalla, and is mainly occupied by the fishermen. We managed to trace only seven out of

the reported 10 cases in this village. The seven cases and 135 village controls were entered in the analysis, the results which suggested a small cluster with 0.06 km radius, rate ratio (O/E) = 7.4, relative risk 15.87 and log likelihood ratio 6.388, which approaches statistical significance level ($P = 0.074$). Figure 5.10 shows the distribution of these cases and village control homesteads as well as the cluster.

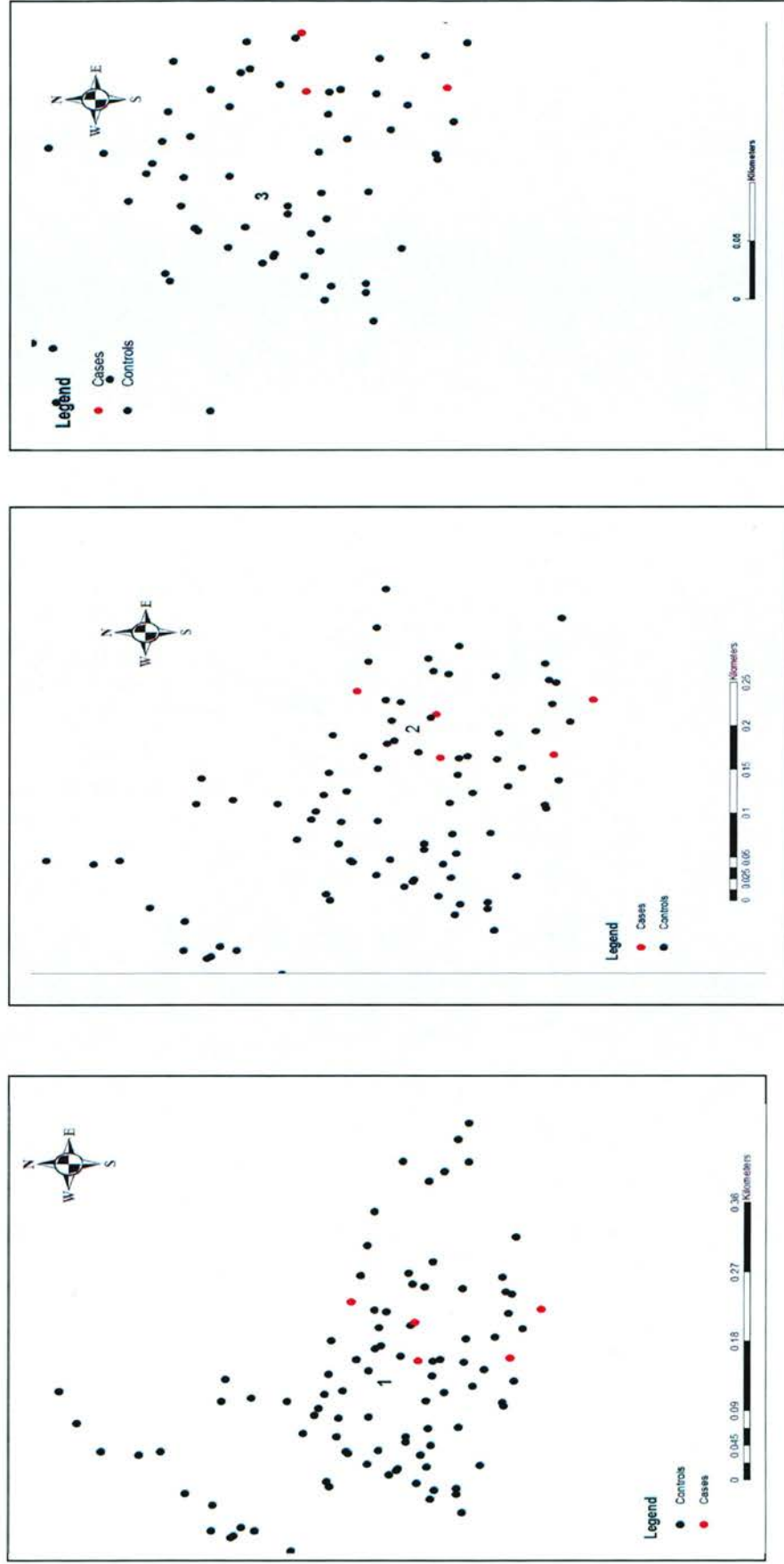
Figure 5.10 Usinga map showing the location of village homesteads in black and sleeping sickness cases marked red.



Note:

Locations 1, 2 and 3 are clearly shown in the following map (Figure 5.10.1

Figure 5.10.1 Usinga homesteads showing cases in red and controls in black

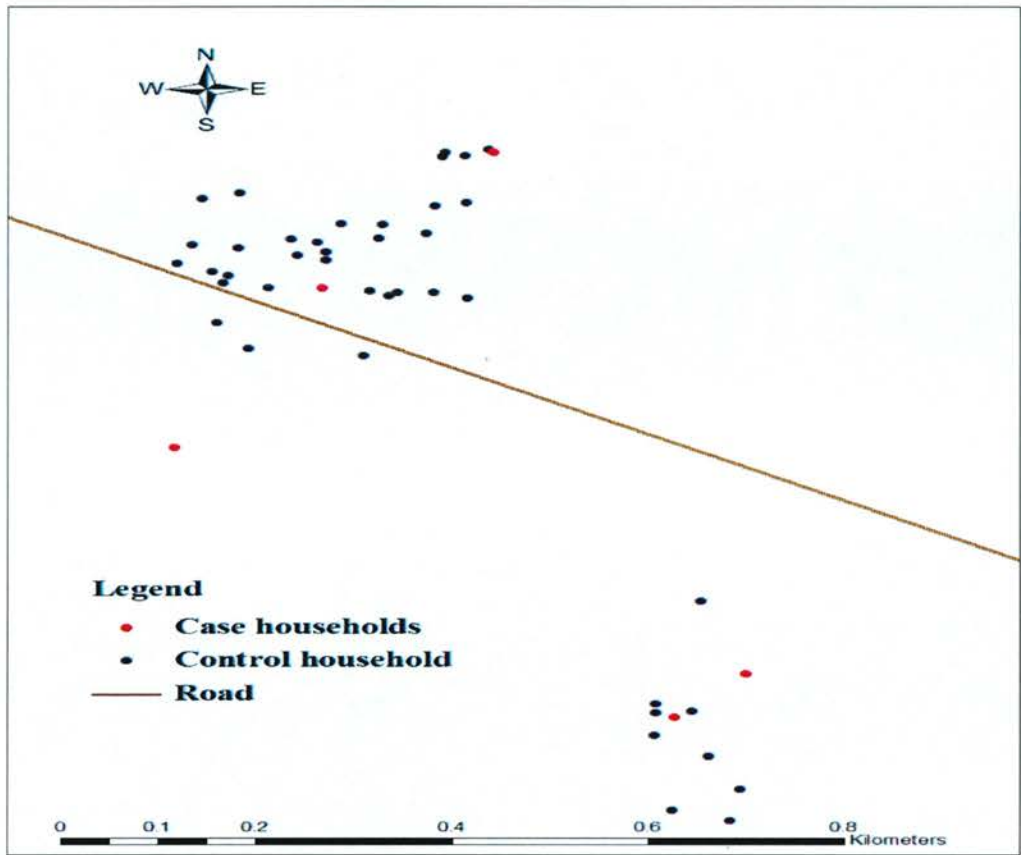


5.3.2.4 Ukumbikakoko village

Ukumbikakoko is the farthest of all the study villages, located 109 km from Kaliua health centre when travelling by train. It is the smallest of all the surveyed villages, and also least populated. It is found on the shores of River Ugalla which divide Urambo and Mpanda districts.

It is occupied mainly by fishermen and small scale subsistence farmers. With exception of train, access to the village is very difficult. Though Ukumbikakoko was not listed in any of the health facilities as having cases of sleeping sickness, it was observed during village level interviews in Usinga that two names reported under Usinga were actually residents of Ukumbikakoko. Ukumbikakoko was visited with the aim of conducting interviews with the two cases and realized that there were three more patients one diagnosed and treated in Tabora and two in Mpanda. The five cases were combined with 81 village controls in the analysis. The results of the analysis (Table 5.2) suggested statistically non significant cluster ($P = 0.421$). Figure 5.11 shows the distribution of the cases and village controls.

Figure 5.11 Ukumbikakoko map showing case and control homesteads

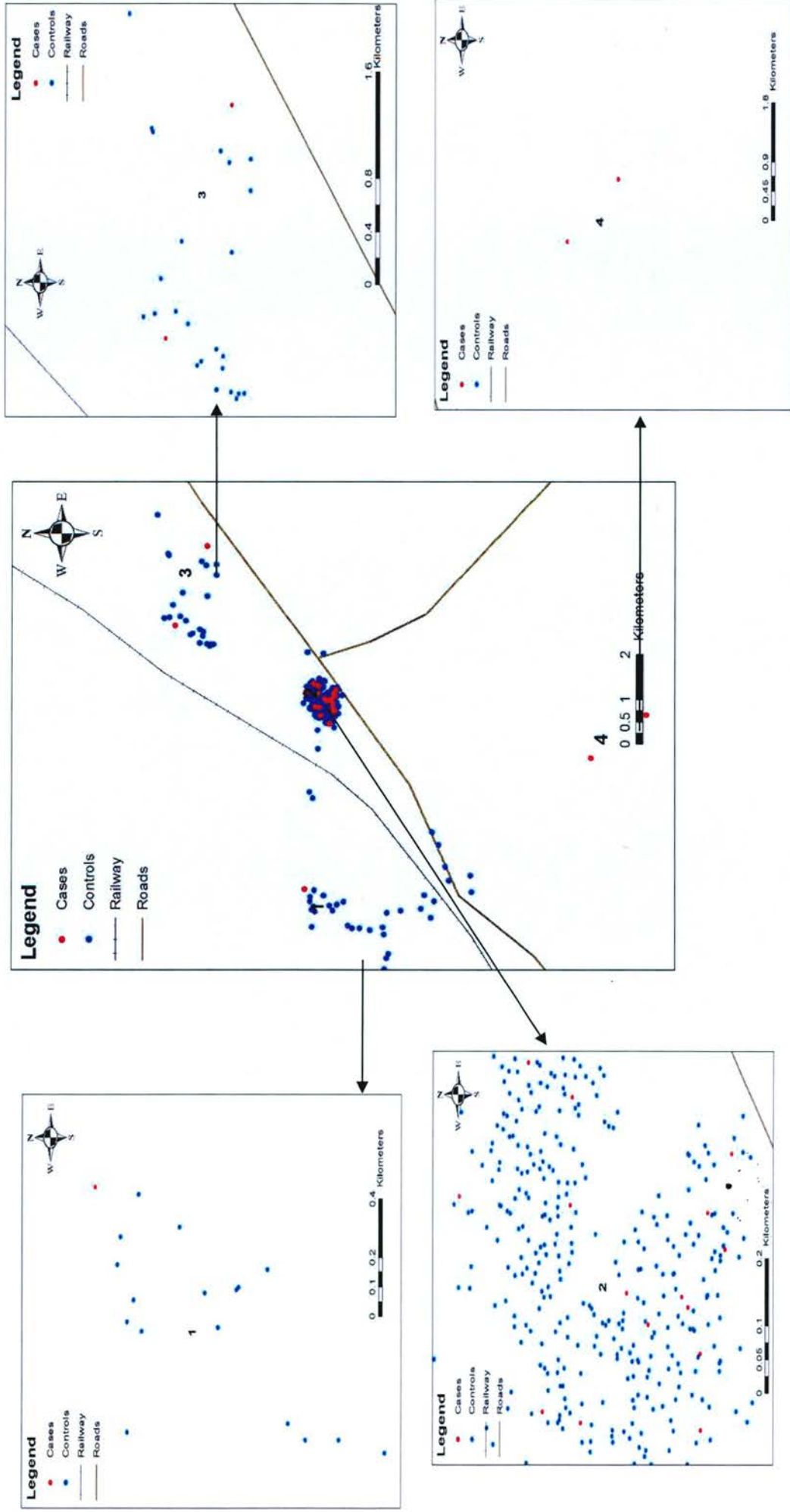


5.3.2.5 Kangeme

Kangeme is among the most severely affected villages in the district, reporting a total of 43 sleeping sickness cases between January 2004 and July 2007.

The team was able to survey all the 483 homesteads in this village, however; only 25 cases out of the 43 reported in the village were traced. Findings of the analysis suggested one most likely cluster ($P = 0.63$), which was statistical not significantly. Figure 5.12 below is a map showing the location of all homesteads for cases and controls.

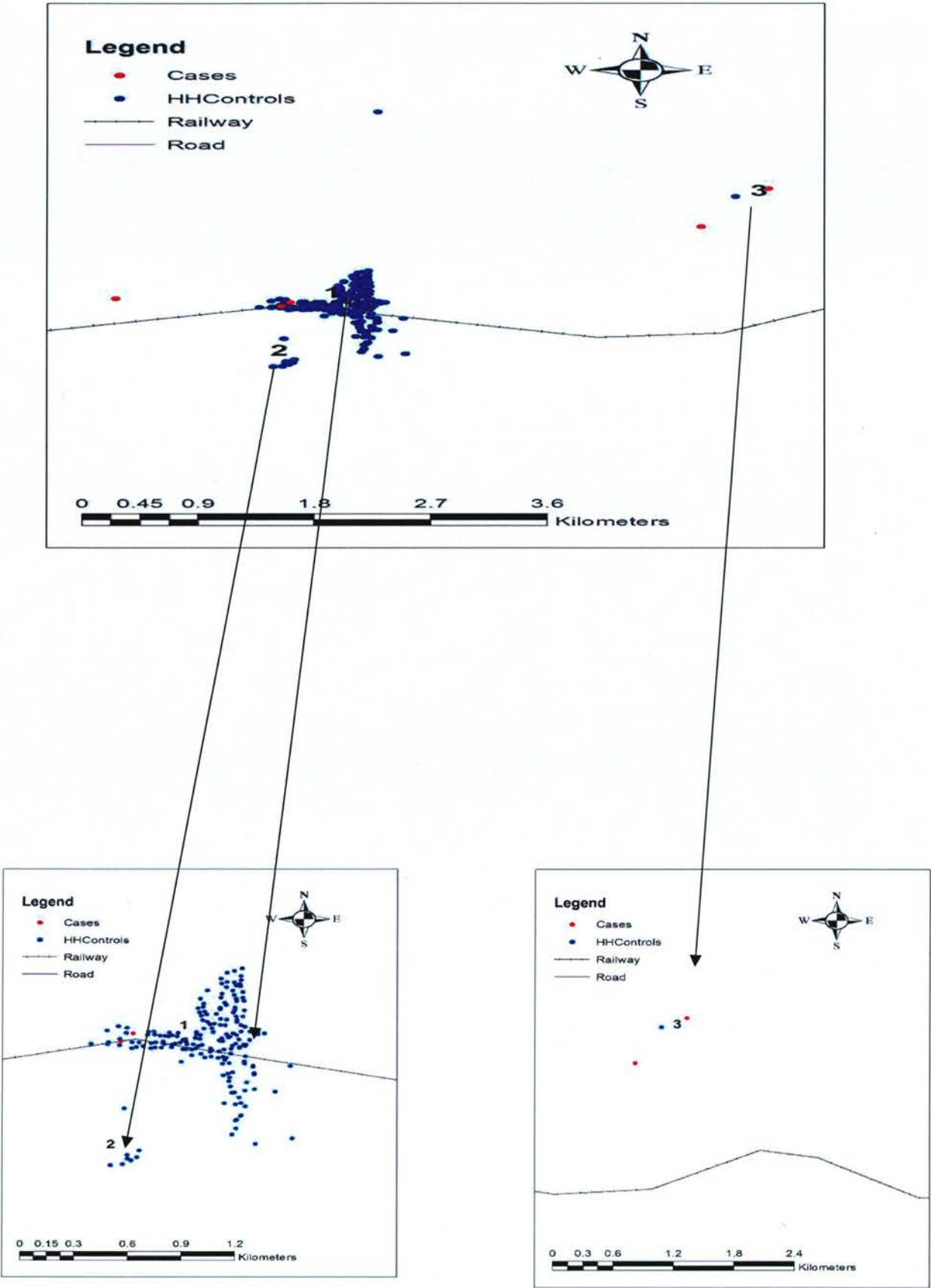
Figure 5.12 Map of Kangeme showing Location of sleeping sickness cases and house control



5.3.2.6 Kombe village

From the hospital records only three cases were listed, three more cases were discovered in the village during the survey and were combined with 195 village controls to make a total of 201 homesteads which were analysed. Results suggested statistically non significant cluster ($P = 0.216$). Figure 5.13 shows the distribution of case and control homesteads in Kombe village.

Figure 5.13 Kombe map showing location of case and control homesteads.



5.4 Socioeconomic and Behavioural Risk Factors

A total of 100 cases and 100 sex, age and place of residence matched controls were selected and surveyed. Interviews were conducted with all these subjects and analysed using methodology described above. The distributions of demographic data for both cases as well as controls are displayed in Table 5.3.

Findings from the current study demonstrated a very strong statistical association between sleeping sickness and the presence of a family member with a previous history of sleeping sickness $P < 0.001$; OR: 6.43 (95% CIs: 2.9 – 14.3). Contact with wild animals in the village was also associated as follows; seeing hyenas $P = 0.005$; OR: 2.89 (95% CI: 1.37 – 6.10), seeing lions in the village $P = 0.01$; OR: 2.49 (95% CI: 1.21 – 5.10), and seeing elephants in the village $P = 0.03$; OR: 2.39 (95% CI: 1.08 – 5.29). Visit to the forest reserve was slightly associated $P = 0.028$; OR: 2.3 (95% CI: 1.09 – 4.83). However, having a knowledge about causes and transmission of sleeping sickness appeared to have a negative association with sleeping sickness infection in the study villages $P = 0.01$; OR: 2.0 (95% CI: 0.86 – 4.67).

Table 5.3 Characteristics of cases and controls

Characteristics	HAT Cases	Population controls
	(No. %)	(No. %)
Sex		
Male	64%	64%
Female	36%	36%
Education level		
Informal	23%	21%
Primary	73%	75%
Secondary	3%	4%
Adult	1%	0%
Occupation		
Farmer	56%	67%
Lumberer	13%	12%
Firewood collection	6%	6%
Honey gathering	3%	2%
Charcoal Burning	8%	5%
Residence		
Lumbe	34%	34%
Kangeme	25%	25%
Ukumbisiganga	18%	18%
Usinga	7%	7%
Kombe	6%	6%
Ukumbikakoko	5%	5%
Usinge	4%	4%
Zugimlole	1%	1%

Table 5.4 Risk factors for human African trypanosomiasis (Univariate-analysis)

Factor	Odds Ratio(OR)	95% CIs	<i>P</i> - Value
Forest visit	2.30	1.09 - 4.8	0.028
SS in the family	6.43	2.9 - 14.3	<0.001
Visit to tsetse area	2.00	0.68 - 5.85	0.190
Seen Lior in the village	2.49	1.21 - 5.10	0.010
Seen Elephants	2.39	1.08 - 5.10	0.031
Seen Hyena	2.89	1.37 - 6.17	0.005
Seen MLizard	2.21	1.17 - 4.17	0.140
Seen Warthogs	1.50	0.81 - 2.78	0.200
Seen Rats	0.65	0.32 - 1.31	0.230
Farming activities far from home	1.20	0.52 - 2.78	0.670
Aware of cause of ss (tsetse)	2.00	0.86 - 4.67	0.110
Keeping livestock at homestead	1.20	0.61 - 2.38	0.600
Cultivate maize	1.40	0.44 - 4.41	0.570

When all significant risk factors were fitted in conditional logistic regression model (multivariate), only having a member of family with previous sleeping sickness history remained highly significant OR: 20.69 (95% CI: 4.79 – 89.33), $P < 0.001$ (Table 5.4). All other factors which were initially significant turned out to be insignificant.

Table 5.5 Risk factors for sleeping sickness in Urambo district, conditional logistic regression model for matched data (Multivariate analysis)

Factor	Adjusted Odds Ratio 95% CI		P- Value
SS in the family	20.69	4.79 - 89.33	<0.001

Figure 5.6 Picture of wild animals (Waterbucks) which was photographed during survey in one of the sleeping sickness endemic villages



5.4 Discussion

This was the first time a study of this kind was conducted in *rhodesiense* sleeping sickness endemic area in an attempt to investigate the possible spatial and behavioural risk factors for *rhodesiense* sleeping sickness in Tanzania. Therefore, based upon previous risk factors studies conducted both in *gambiense* and *rhodesiense* sleeping sickness endemic areas in other sub-Saharan African countries (Meda *et al.*, 1993; Okia *et al.*, 1994; Robays *et al.*, 2004; Welburn *et al.*, 2006), a wide range of potential factors which were reported to be associated with an increased risk of sleeping sickness transmission, were examined and considered while designing this survey.

Results of the current study demonstrated a very strong clustering of *rhodesiense* sleeping sickness endemic villages in Urambo district. The clustering was observed only at the village level analysis ($P < 0.001$). The model also suggested a possibility of having clustering at within village analysis in all six surveyed villages; however, statistically there was no significant association in any of the suggested clusters. This means that clustering in Urambo is only limited at the village level, and localized to specific parts of the district, particularly in villages bordering Kigoma rural and Mpanda districts which are also covered in the cluster.

These findings were not unexpected as the homogeneous distribution of sleeping sickness cases in all the villages surveyed was also observed during the mapping exercise. These findings suggest that, residing in any of these villages is a risk itself rather than having a specific activity in the village. Hence village residents are exposed to risk of being infected with sleeping sickness. This means that all residents of the six surveyed villages have an equal chance of sleeping sickness infection.

Having a family member with previous history of sleeping sickness was also found to be associated with increased risk of sleeping sickness in the district.

This findings are consistent with earlier risk factor studies conducted both in *rhodesiense* (Okia *et al.*, 1994), and also findings of a more recent study conducted in South East Uganda (Zoller *et al.*, 2008), as well as another study conducted in *gambiense* sleeping sickness endemic areas (Gouteux, 1988). In all these studies the authors suggested that the probable explanation for this finding is that, families tend to share similar patterns of risk activities, they also suggested that biting by infected tsetse may be occurring around homesteads. Given the fact that several studies have now observed this finding is a serious challenge to researchers. On the other hand it opens a door for further studies, to investigate the potential genetic factors existing among family members in HAT affected families, which are likely to play role in increasing susceptibility to infection. Studying host-parasite genetic interaction has been suggested to be considered as important tool for eradication campaigns (Garcia *et al.*, 2006). Another possible reason which may be suggested is that there is an increased awareness in regarding clinical presentation among family members with previous HAT patients, which forces patients to seek medical attention as soon as they see similar clinical presentation, this increases the chances of been diagnosed early.

Contrary to the authors expectations, the current study found no statistical association with a number of high risk activities conducted in the study area; such as firewood collection, lumbering, fishing and honey gathering, despite the fact that honey gathering came out clearly as one of the potential activity which forces people to encroach on the forest. Most of the older study cases (age between 40-80 years) were involved in honey gathering activities, which forces them to enter and spend a number of days inside the forest reserve. Results of this study should not in any way be used to draw any conclusion as they do not exclude the possibility of honey gathering or any of the activities mentioned above being potential risk factors in future studies or in other areas of Tanzania. The probable explanation for non

statistical association in any of the studies activities is that all mentioned activities were homogenously distributed among both cases and controls in the study villages.

A risk factor study conducted in Cameroon (Grebaut, 2001), observed significant association between hunting and sleeping sickness transmission. In this study it was difficult to capture this factor in any of the study villages. Hunting in Urambo is restricted to permit holders only, with most of the hunting activities conducted by private companies, both local and international. The companies would normally hire professional hunters and for short periods mostly during dry season when most of the hunting activities are conducted. Most professional hunters, the study team came across during survey were temporary residents and did not meet the study criteria which was to have lived in the study area for two or more years. Most of the study villages were considered to be almost inaccessible during rainy seasons, as all major roads in the district are unpaved and majority are in very bad shape. Surprisingly, almost all the study villages are accessible by train throughout the year, but it is unlikely that the some of the risky activities such as hunting would be conducted during the rainy season for security reasons. The fact that all hunting activities require one to have a hunting permit does not exclude possibilities of illegal hunting by poachers, although it was not possible to verify this fact, as none among the study subjects was identified to conduct hunting activities.

A very similar study conducted recently in Uganda (Zoller *et al.*, 2008), observed significant clustering in five out of six survey villages. The spatial risk factors identification in both studies is important aspect as it may contribute towards reducing the number of costs in future control programmes. To achieve this goal the policy markers may need to consider targeting specific focal areas instead of allocating the resources throughout the entire endemic area. For this particular case for example it is obvious that deploying tsetse impregnated targets in any of the six villages will not produce the desired impact in the control of tsetse, instead they should be

targeted to specific areas, where there is obvious increased man-tsetse contact such as watering points and areas of increased forest activities.

Studies conducted elsewhere (Odiit *et al.*, 2004) observed association between *rhodesiense* HAT and water sources [Odiit, 2005, Zoller, 2008] however, in the current study it was not possible to establish this association as most of the surveyed homesteads are located very close to one another (about two to five minutes walk). Apparently there was no common source of water supply which could be regarded as a meeting point which would have increased the risk of tsetse fly bite in any of the surveyed villages. In most cases people use water from shallow wells which were observed in some of homesteads particularly in homes which are located near or inside reserve forest. The only reliable source of water was observed in the villages located along Ugalla River, which is very wide and can be accessed in several points and hence no single area could be regarded as a single common point.

The results of the univariate analysis which are explained in this chapter also suggested that wildlife are the possible risk for the current resurgence of sleeping in Urambo district, meaning that probably the disease is still been transmitted in a traditional way as compared to what has been happening in other regions of *rhodesiense* HAT. This finding fits well to the hypothesis made by Fairbain (1948) who suggested that the 1922 -1948 HAT epidemic in Tanzania was probably the spill-over infection from wild animal reservoirs to humans (Fairbairn, 1948).

During the village level discussion, some of the village elders associated presence of sleeping sickness with the existence of wild animals particularly elephants and this was repeatedly mentioned in different study villages. This study was however not able to confirmed this association, as wild animals which appeared to be potential risk factors for sleeping sickness in univariate analysis were eliminated by multivariate analysis.

It is well understood that animals are the preferred hosts by tsetse flies when compared to humans, and also most of the wild animals including elephants, enter the villages late at night when tsetse flies are not present, it is suspected that the remains of animal dung and the smell of their urine may attract some tsetse to these villages, posing possible risk to population. Documented research findings show that, odours released by tsetse's natural host may act as a potential attractants for tsetse flies (Späth, 1997).

The finding that wild animals could still play a big part in the transmission of sleeping sickness in Tanzania is a serious and biggest challenge, given a large number of wild animals in game reserves and National Parks all over the country and particularly, in the western and south western parts of Tanzania where the disease has always been endemic, also where it has re-emerged in recent years (Kibona 2001).

The study noted that the residents in all surveyed villages keep a very small number of domestic animals in their catchment areas, despite the district's richness in grazing land. When asked to comment on this, the local residents explained the reason preventing them from keeping livestock is basically the dangers of tsetse flies as well as wild animals such as lions and leopards. Tsetse fly abundance was also listed in regional profile as the main reason preventing livestock keeping in the district (RALG, 2007). It was also noted that apart from government effort to control the disease, several other parties are playing part in the control of the disease, the only problem observed is lack of coordination between these parties and the experts, this is due to the fact that some of the control measures placed did not follow the recommended standards, the good example is the target in figure 5.6 which is made of green and blue colour instead of the recommended colours which are blue and black (Vale and Torr, 2004). The blue colour act as a visual attractant to tsetse flies and the black colour forms the main alighting surface (Leverssière *et al*, 1990).

It was, however, observed that there were markedly large numbers of livestock movements in the district. Pastoralists from Shinyanga, Kahama and Mwanza travel on foot with large numbers of herds through dense forests of Urambo, particularly during the dry season. These pastoralists travel to Mpanda to secure grazing areas for their herds. There is a high chance that the increased number of sleeping sickness cases in Urambo as well as Mpanda were re-introduced through this route, as the forest reserve is heavily infested with tsetse flies, as seen in Figure 5.1.

Domestic animals particularly cattle are known to be potential reservoirs for sleeping sickness (Onyango *et al.*, 1966). While a study conducted in Uganda highlighted the importance of cattle movement as the potential risk for sleeping sickness transmission (Welburn *et al.*, 2006). Effective control options can only be achieved by considering direct efforts to be targeted to the protection of the livestock. The only possible cost-effective option for the rural settings is the use of restricted insecticide application (Eisler *et al.*, 2003), to all livestock travelling through forest reserve, as well as use of insecticide treated tsetse control techniques may offer a better option in intervening the wildlife-domestic transmission cycles.

CHAPTER SIX

GENERAL DISCUSSION

6.0 General Discussions

Trypanosomiasis is known to have existed in the western part of Tanzania for over eighty years. Despite this part of the country having some of the oldest active HAT foci, over recent years, little has been achieved in terms of understanding the actual disease magnitude in the country; the main reason for this has been the lack of sufficient and sustainable funds for research. Compounding this scenario is that there has been no national HAT control programme in the country which could aid in validating epidemiological dynamics. This thesis therefore attempted to investigate the epidemiology of HAT in western Tanzania, as a way of gathering some baseline information which in future will provide an insight of the disease situation and hence contribute towards better planning of control interventions. Hence in Chapter II, findings of a historical review suggested that both forms of HAT probably existed in Tanzania in the past, although at present time only Rhodesian sleeping sickness is reported to exist in the country. It is possible that Gambian sleeping sickness was present in the past. The introduction of *T. b. gambiense* into Tanzania was believed to originate from the Belgian Congo (now Democratic Republic of Congo (DRC)) and occurred mainly at the shores of Lakes Victoria and Tanganyika.

Chapter III assessed the level of sleeping sickness under-reporting in Urambo district, Tanzania and suggested that HAT under-reporting is extremely high, and it is clear that considering the remoteness of communities affected with the disease, and the unavailability of sufficient health facilities with the capacity to manage the disease (Malele *et al.*, 2006), it is clear that most of the sleeping sickness cases are always missed and die probably undiagnosed in rural communities. Clearly, given the seriousness and extent of sleeping sickness under-reporting and also due to the fact that all under-reported cases did not attend any health facility meaning were not diagnosed and therefore receive no treatment, these are assumed to be unreported deaths (sleeping sickness is invariable fatal if no treatment is provided).

Findings of under-reporting were incorporated into chapter IV which deals with the quantification of the burden of disease due to *rhodesiense* sleeping sickness in the country, and hence the DALY scores for rhodesiense sleeping sickness in Tanzania were determined. Findings which show significant burden are imposed by HAT to local communities as well as health care systems.

In order to be able to properly plan control strategies for any particular disease, it is important to understand the disease trends in that particular area. During the literature review and also the historical review of existing HAT records, it was discovered that no previous study had been conducted in Tanzania to investigate the factors which may have contributed towards human African trypanosomiasis transmission and maintenance. Therefore using combination of tools and techniques, Chapter V of this thesis attempted to fill this gap by conducting a matched case control study both at the village and within village scales. This enabled for the first time to establish both spatial and behavioural risk factors for HAT in Urambo district, Tanzania. The study observed that apart from risk factors identification, the significant level of poverty observed in the district is attributable partly to the very small scale level of subsistence farming conducted in the district, which basically uses very poor tools. Lack of livestock keeping behaviour observed among the villagers which may seem to be a positive factor as far as HAT transmission and maintenance is concerned, and also regardless the fact that domestic animals were not identified as a possible risk factor for HAT in this thesis, a significant number of livestock movement was reported by residents of all the study villages, which were reported to be transported between two neighbouring districts Shinyanga and Mpanda passing through Urambo, also a large number of different species of wild animals were reported to enter habitants. Animal movement have been identified as an important risk factor for zoonotic HAT in other east African countries (Fevre *et al.*, 2006a)

It is, however, strongly advised that the findings of this thesis be treated with caution and should not under any circumstances be generalized for other HAT endemic districts of Tanzania. The main reason for this is that Urambo has a completely different scenario as compared to rest of the country.

It is probably one of the poorest districts of Tanzania in terms of infrastructure and gross national income (GNI) ranking, all its roads (urban and rural) are unpaved and the villages are located far apart from one another and it is the district with probably the worst health facility coverage in the country. Also the type of agricultural activities and crops which are cultivated are different from other disease endemic districts and it is the district with probably the largest mixture of different ethnic groups in the country, about 17 different ethnic groups were identified during this study. In view of all above listed findings it is unlikely that the studies from other districts will necessarily follow similar disease patterns to that found in Urambo district.

6.1 Disease Control Measures

HAT continues to be recorded in Tanzania (Kibona 2001) and the evidence from this study shows that new villages have been reporting sleeping sickness. This suggests that there is an urgent need to investigate the actual disease situation in order to be able to plan long term control programmes, as well as strengthening the existing surveillance activities. Historically, gambiense sleeping sickness is believed to have occurred in Tanzania in the past. Although the disease situation before World War I is not very clear, some cases are believed to have occurred during German rule. However, it is unlikely that gambiense HAT has ever been endemic in the country, with the epidemic rhodesiense driven largely by human contact with animal hosts either domestic or wild. Tanzania needs to remain vigilant about the possibilities of re-introduction of *T. b. gambiense*. The chances of gambiense sleeping sickness being reintroduced into the country still exist, particularly in the areas where transmissions were observed in the past on the shores of Lake Tanganyika particularly on the DCR border. The finding that patient's medical records are destroyed after 10 years is unacceptable; patient's data need to be protected, as this will allow proper tracking of patient's medical history.

Therefore there is an urgent need for the responsible administrative units to unite efforts and design effective and sustainable means of storage of medical data.

Wild animals play an important role in maintaining Rhodesian sleeping sickness in areas where the disease is endemic.

During the current work wild animals were suggested to be important risk factor for HAT with most of the villages surveyed being sited inside forest reserves and/or protected areas where they interact with wild animals on a daily basis. Besides it was observed that there is a large abundance of tsetse flies in human populated areas with the communities also reporting that apart from tsetse flying freely in their residential areas, a large number of wild animals were seen in the villages as well as in the farms. This is a big concern, as apart from contributing to increase poverty in the area by destroying crops, the presence of wild animals increases the chances of sleeping sickness transmission as well as causing danger to humans as there were some reports of humans been attacked and been injured by wild animals such as lions. So instead of placing HAT control interventions such as targets randomly inside the forest, it is advised to direct control interventions such as insecticide impregnated targets to targeted areas such as areas with increased tsetse-animal and tsetse-human contacts such as watering points, along the paths to farms, particularly those which are located close to or inside forest reserves, and along busy roads. This is probably the most cost effective way of reducing the chances of humans coming into contact with infected tsetse flies and will play an important role in reducing the abundance of tsetse flies in the area, it will also be easier to maintain the targets and prevent their constant destruction by wild animals.

6.2 Policy Implications

Recently, a number of studies have found that case detection and treatment provision to humans may not be sufficient in controlling *rhodesiense* sleeping sickness in most of the

affected countries. This is partly due to the large number of animal reservoirs which play a pivotal role in the transmission and maintenance of the disease in respective areas.

This thesis therefore suggests several policy implications, first lowering physical distance between villages and health facilities with the capacity to manage HAT, This may contribute towards increasing the numbers of early case detection resulting in proper treatment, hence reducing the amount of under-reporting and mortalities.

Secondly, improving the quality of care in the available health facilities, by equipping these facilities with sufficient manpower and supplies, this may play a vital role in reducing the burden imposed to local communities, improving the infrastructure such as roads may allow easy transportation to treatment centres throughout the year, hence reduce the amount of under-reporting caused by poor access to centres with capacity to manage the disease. Screening, treatment provision and providing prophylactic measures such as pour-on to all livestock transported through these villages may assist in reducing the number of transmissions caused by these animals. Finally awareness creation to people living in these communities on the risk posed to them by tsetse flies as well as animal reservoirs.

6.3 Way Forward

Apart from being one of the most neglected diseases, HAT is severely under-reported in most of the disease endemic countries. This thesis managed to establish the level of HAT under-reporting in Tanzania using a decision tree model which was developed for Uganda (Odiit *et al.*, 2005) This was done as way of getting an overview of what the situation may look like in Tanzania, assuming that the disease follows the same patterns across east Africa. One of the initial steps in planning the way forward of this thesis is to develop a model which will be specific for Tanzania.

The most important concerns in sleeping sickness under-reporting and in general in HAT control is lack of easily accessible, affordable and sensitive diagnostic tools which can be considered as pen side and can be easy to use in most of disease endemic rural areas of Tanzania. Todate, the only method which is regarded as the gold standard for HAT diagnosis relies on microscopy which is not sensitive enough. Besides, most of the good quality microscopes which are currently available in the market require stable power source which is again is a big concern as is not available in most of the disease endemic rural communities of Tanzania. Even so, in areas where electricity is available the power supply is not always stable as the currently used power in Tanzania relies mostly on hydropower.

Given fluctuations in weather condition, power rationing is obviously an unavoidable obstacle. However, recently developed Loop-mediated isothermal amplification (LAMP) has shown to provide a suitable option for this (Notomi *et al.*, 2000)

In this thesis the risk factors for HAT in Urambo were established, though the aim of this thesis is not to generalize the findings of Urambo to the rest of Tanzania. Most of the findings may play important role in other parts of the country as they have been reported in other countries as well. Although this thesis did not establish any direct link or any evidence of direct association between domestic animals and current disease resurgence in the study area The fact that among other things there is an increased number of livestock movements in the area during the dry season, is an important finding as it calls for an urgent need to conduct intensive studies in the area so as properly investigate the role played by both wild and domestic animal reservoirs in transmitting as well as maintaining the disease in the area. It is also useful to try and properly investigate the areas of disease transmission as this will suggest areas needing special attention for future control programs.

There is also an urgent need to conduct studies on tsetse distribution, particularly in areas where *gambiense* HAT occurred in the past. In order to update the existing epidemiological data, it is also fundamentally important to properly investigate the actual

disease magnitude for both *rhodesiense* and *gambiense* sleeping sickness in the western part of Tanzania.

It is also proposed to conduct another risk factor investigation in another district of Tanzania where the disease is endemic in order to compare the findings and allow proper planning of control interventions.

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APPENDIX 1

QUESTIONNAIRE FOR TANZANIA

PART 1

(Individual questionnaire)

1.0. Respondent Particulars

1.1. Name of respondent.....GPS of h/hold S.....E.....A.....

1.2 Case/control.....

1.3 Date of interview.....

1.4 Age

1.5 Sex:

1.6 Tribe.....

1.7 Level of Education

1. Informal
2. Primary
3. Secondary
4. Tertiary
5. Adult

1.8 Relationship of case/control to respondent.....

1.9 Main occupation

1. Farmer

2. Rail worker

3. Hunter

4. Businessperson

5. Fisherman

6. Student

7. Others (specify).....

Any other occupation (Specify) if more than one occupation.

1.10 Village/sub-village (Kitongoji).....

1.11 Distance from nearby h/facility (est. hours it will take to walk).....

1.12 Distance from your home to the village centre.....

1.13 Distance from the nearest neighbour.....

1.14 Ward

1.15 District.....

1.16 GPS coordinates of village centre: Long Lat..... Alt

1.17 How much does it cost to travel to the Health Centre.....

2.0 Knowledge of the disease

2.1. Are you aware of any disease that affects both humans and animals? 1. Yes

2.No

If yes, please mention three most important ones

1.....

2.....

3.....

2.2. Can you mention any disease that is caused by tsetse fly bite?

1.....

2.....

2.3 Please mention the names of the areas where you find most of tsetse flies in your village

.....

.....

.....

.....

2.4 How long will it take you to walk to that place

2.5 have you ever visited that place? ☐ Yes ☐ No

2.6 Does your community member take any actions to control the tsetse flies?

☐ Yes ☐ No

If yes please mention any two;

.....

.....

2.7 Please mention the areas where your family members carry out the following activities

- 1. Farming
- 2. Herding animals.....
- 3. Wood cutting/collecting.....

2.8 How far is the forest reserve from your house (est. time taken by walking)

2.9 Which of the following wild animals do you see in your village? (Household)

Animal specie	Very often	Occasionally	Never
Hyenas (Fisi)			
Warthogs			
Wild beast			
Dick dick			
Impala			
Elephants			
Lion			
Monkeys			
Monitor lizard (Kenge)			
Others			

2.10 Can you describe activities carried by your family members?

1. Wife/Husband.....
2. Son.....
3. Daughter.....
4. Attendant.....
5. Other (specify relationship).....

2.11 Mention areas you visited outside your area/village in the past three months

Village..... Ward/district.....time spent.....

.....

.....

Reason for the visit.....

.....

2.12. Please mention the diseases you suffered over the past one year

1.....

2.....

3.....

2.13. Have you or any of your family members ever suffered from SS?

1. Yes () 2. No ()

If yes, please answer the following:

Name.....

When was it (month/ year)..... Age.....

Occupation.....Outcome.....

2.14. Please describe the cattle movement patterns in your village

FromTo..... Period.....

3.0 Socioeconomic Assessments

3.1. Which and how many of the following do you keep in this homestead? Please tick yes or no and provide the quantity (Household)

Animal	Yes	No	Amount /quantity
Cows			
Goat			
Sheep			
Pigs			
Chicken			
Ducks			
Others (specify)			

3.2 Please record the number of people in each age group who live in your household including your self, spouse, children servants and any other relatives

- 0 – 5 years.....
- 6 -15 years.....
- 16- 29 years.....
- 30 – 44 years.....
- 45 – 59 years.....
- 60 & above.....

3.3. Do you own any of the following? (Household/individual)

Item	Yes	No	Amount/quantity
Land			
House/shelter			(No. of rooms)
Vehicle			
Tractor			
Plough			
Shop			
Bicycle			
Others (specify)			

3.4. Please mention sources of income for your family (start with order of higher income)

1..... 2.....
3..... 4.....

If farming is among the source of family income, then answer the following question (if is not then move to question 3.6)

3.5. You have mentioned farming as a one of source of your family income, please estimate the amount and value of for each crop (in case farming is not listed then skip this question)

Product (crop)	Amount	Estimated value

3.6. Have you conducted any of the following the following activities over the past one year?

Activity	Time conducted (month)	Area where conducted
Agriculture		
Hunting		
Honey gathering		
Lumbering		
Fishing		
Charcoal burning		
Firewood collection		
Travel out of the village		

3.7 Assessment and recording the condition of the household of the case/control basing on the following criteria a: structure; roof type: type of latrine (tick according to your observations)

Household structure	Roof type	Latrine
..... Mud Iron sheet In-door
..... Timber/wood Grass thatch Pit
..... Cement Tiles None
..... Any other Other	

3.8 Have you ever visited the forest reserve? ☐Yes ☐No

If yes how often do you go to the forest.....

What is the main reason for the visit.....

3.9 have ever visited the forest during the night ☐Yes ☐No

If yes how often do you go there.....in a week.....in a month.....

PART 2

(Village level questionnaire)

1. Where do you find tsetse flies in your village?

Area	Quantity (L/M/H)	Distance from village centre	Action taken to control them	Time action taken

2. Can you describe the activities carried out by village members?

Activity	Who perform the activity; sex, age group	Area where the activity is performed	Time spent to perform the activity

3. What kinds of crops do people in this village grow?

.....
.....
.....

4. Do you see wild animals in your village? 1. Yes 2. No

If yes then please answer the following

Type of animal..... Area where found.....

.....

.....

.....

.....

5. Do you have cattle market in this village? ☐ Yes ☐ No

If yes, please name it.....

Where is it

Distance from village centre.....

If no then which nearest cattle market in this area.....

6. Do you have any migration of people into or out of your village over the past 2 years?

.....

7. Do you have any herds' migration in or out of your village over the past two years?

If the answer for questions 5 or 6 is yes then what was the reason for

migration.....

8. Please describe cattle movement pattern in your village?

FromTo.....period.....

From.....To.....period.....

9. Please explain what do you think was the main reason for this movement

.....

.....